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#### (54) Title: SYNTHETIC PEPTIDES AND USES THEREFORE

(57) Abstract: A synthetic polypeptide is disclosed, which comprises a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Synthetic polynucleotides are also disclosed that code for the synthetic polypeptides of the invention as well as expression constructs comprising the synthetic polynucleotides. Also disclosed are methods for constructing the aforementioned molecules and immunopotentiating compositions and methods for treating and/or preventing a disease or condition.



#### SYNTHETIC PEPTIDES AND USES THEREFORE

#### FIELD OF THE INVENTION

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THIS INVENTION relates generally to agents for modulating immune responses. More particularly, the present invention relates to a synthetic polypeptide comprising a plurality of different segments of a parent polypeptide, wherein the segments are linked to each other such that one or more functions of the parent polypeptide are impeded, abrogated or otherwise altered and such that the synthetic polypeptide, when introduced into a suitable host, can elicit an immune response against the parent polypeptide. The invention also relates to synthetic polynucleotides encoding the synthetic polypeptides and to synthetic constructs comprising these polynucleotides. The invention further relates to the use of the polypeptides and polynucleotides of the invention in compositions for modulating immune responses. The invention also extends to methods of using such compositions for prophylactic and/or therapeutic purposes.

Bibliographic details of various publications referred to in this specification are collected at the end of the description.

#### **BACKGROUND OF THE INVENTION**

The modern reductionist approach to vaccine and therapy development has been pursued for a number of decades and attempts to focus only on those parts of pathogens or of cancer proteins which are relevant to the immune system. To date the performance of this approach has been relatively poor considering the vigorous research carried out and the number of effective vaccines and therapies that it has produced. This approach is still being actively pursued, however, despite its poor performance because vaccines developed using this approach are often extremely safe and because only by completely understanding the immune system can new vaccine strategies be developed.

One area that has benefited greatly from research efforts is knowledge about how the adaptive immune system operates and more specifically how T and B cells learn to recognise specific parts of pathogens and cancers. T cells are mainly involved in cell-mediated immunity whereas B cells are involved in the generation of antibody-mediated immunity. The two most important types of T cells involved in adaptive cellular immunity

are αβ CD8<sup>+</sup> cytotoxic T lymphocytes (CTL) and CD4<sup>+</sup> T helper lymphocytes. CTL are important mediators of cellular immunity against many viruses, tumours, some bacteria and some parasites because they are able to kill infected cells directly and secrete various factors which can have powerful effects on the spread of infectious organisms. CTLs recognise epitopes derived from foreign intracellular proteins, which are 8-10 amino acids long and which are presented by class I major histocompatibility complex (MHC) molecules (in humans called human lymphocyte antigens - HLAs) (Jardetzky et al., 1991; Fremont et al., 1992; Rotzschke et al., 1990). T helper cells enhance and regulate CTL responses and are necessary for the establishment of long-lived memory CTL. They also inhibit infectious organisms by secreting cytokines such as IFN-y. T helper cells recognise epitopes derived mostly from extracellular proteins which are 12-25 amino acids long and which are presented by class II MHC molecules (Chicz et al., 1993; Newcomb et al., 1993). B cells, or more specifically the antibodies they secrete, are important mediators in the control and clearance of mostly extracellular organisms. Antibodies recognise mainly conformational determinants on the surface of organisms, for example, although sometimes they may recognise short linear determinants.

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Despite significant advances towards understanding how T and linear B cell epitopes are processed and presented to the immune system, the full potential of epitopebased vaccines has not been fully exploited. The main reason for this is the large number of different T cell epitopes, which have to be included into such vaccines to cover the extreme HLA polymorphism in the human population. The human HLA diversity is one of the main reasons why whole pathogen vaccines frequently provide better population coverage than subunit or peptide-based vaccine strategies. There is a range of epitopebased strategies though which have tried to solve this problem, e.g., peptide blends, peptide conjugates and polyepitope vaccines (ie comprising strings of multiple epitopes) (Dyall et al., 1995; Thomson et al., 1996; Thomson et al., 1998; Thomson et al., 1998). These approaches however will always be sub optimal not only because of the slow pace of epitope characterisation but also, because it is virtually impossible for them to cover every existing HLA polymorphism in the population. A number of strategies have sought to avoid both problems by not identifying epitopes and instead incorporating larger amounts of sequence information e.g., approaches using whole genes or proteins and approaches that mix multiple protein or gene sequences together. The proteins used by these strategies

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however sometimes still function and therefore can compromise vaccine safety e.g., whole cancer proteins. Alternative strategies have tried to improve the safety of vaccines by fragmenting the genes and expressing them either separately or as complex mixtures e.g., library DNA immunisation or by ligating such fragments back together. These approaches are still sub-optimal because they are too complex, generate poor levels of immunity, cannot guarantee that all proteins no longer function and/or that all fragments are present, which compromises substantially complete immunological coverage.

The lack of a safe and efficient vaccine strategy that can provide substantially complete immunological coverage is an important problem, especially when trying to develop vaccines against rapidly mutating and persistent viruses such as HIV and hepatitis C virus, because partial population coverage could allow vaccine-resistant pathogens to reemerge in the future. Human immunodeficiency virus (HIV) is an RNA lentivirus virus approximately 9 kb in length, which infects CD4<sup>+</sup> T cells, causing T cell decline and AIDS typically 3-8 years after infection. It is currently the most serious human viral infection. 15 evidenced by the number of people currently infected with HIV or who have died from AIDS, estimated by the World Health Organisation (WHO) and UNAIDS in their AIDS epidemic update (December 1999) to be 33.6 and 16.3 million people, respectively. The spread of HIV is also now increasing fastest in areas of the world where over half of the human population reside, hence an effective vaccine is desperately needed to curb the 20 spread of this epidemic. Despite the urgency, an effective vaccine for HIV is still some way off because of delays in defining the correlates of immune protection, lack of a suitable animal model, existence of up to 8 different subtypes of HIV and a high HIV mutation rate.

A significant amount of research has been carried out to try and develop a vaccine capable of generating neutralising antibody responses that can protect against field isolates of HIV. Despite these efforts, it is now clear that the variability, instability and inaccessibility of critical determinants on the HIV envelope protein will make it extremely difficult and perhaps impossible to develop such a vaccine (Kwong et al., 1998). The limited ability of antibodies to block HIV infection is also supported by the observation that development of AIDS correlates primarily with a reduction in CTL responsiveness to HIV and not to altered antibody levels (Ogg et al., 1998). Hence CTL-mediated and not antibody-mediated responses appear to be critical for maintaining the asymptomatic state

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in vivo. There is also some evidence to suggest that pre-existing HIV-specific CTL responses can block the establishment of a latent HIV infection. This evidence comes from a number of cases where individuals have generated HIV-specific CTL responses without becoming infected and appear to be protected from establishing latent HIV infections despite repeated virus exposure (Rowland-Jones et al., 1995; Parmiani 1998). Taken together, these observations suggest that a vaccine capable of generating a broad range of strong CTL responses may be able to stop individuals from becoming latently infected with HIV or at least allow infected individuals to remain asymptomatic for life. Virtually all of the candidate HIV vaccines developed to date have been derived from subtype B HTV proteins (western world subtype) whereas the majority of the HIV infections worldwide are caused by subtypes A/E or C (E and A are similar except in the envelop protein)(referred to as developing world subtypes). Hence existing candidate vaccines may not be suitable for the more common HIV subtypes. Recently, there has been some evidence that B subtype vaccines may be partially effective against other common HIV subtypes (Rowland-Jones et al., 1998). Accordingly, the desirability of a vaccine still remains, whose effectiveness is substantially complete against all isolates of all strains of HIV.

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#### SUMMARY OF THE INVENTION

The present invention is predicated in part on a novel strategy for enhancing the efficacy of an immunopotentiating composition. This strategy involves utilising the sequence information of a parent polypeptide to produce a synthetic polypeptide that 5 comprises a plurality of different segments of the parent polypeptide, which are linked sequentially together in a different arrangement relative to that of the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the synthetic polypeptide is different to a sequence contained within the parent polypeptide. As more fully described hereinafter, the present strategy is used advantageously to cause significant disruption to the structure and/or function of the parent polypeptide while minimising the destruction of potentially useful epitopes encoded by the parent polypeptide.

Thus, in one aspect of the present invention, there is provided a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

In one embodiment, the synthetic polypeptide consists essentially of different segments of a single parent polypeptide.

In an alternate embodiment, the synthetic polypeptide consists essentially of 20 different segments of a plurality of different parent polypeptides.

Suitably, said segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide.

Preferably, at least one of said segments comprises partial sequence identity or homology to one or more other said segments. The sequence identity or homology is 25 preferably contained at one or both ends of said at least one segment.

In another aspect, the invention resides in a synthetic polynucleotide encoding the synthetic polypeptide as broadly described above.

According to yet another aspect, the invention contemplates a synthetic construct comprising a said polynucleotide as broadly described above that is operably linked to a regulatory polynucleotide.

In a further aspect of the invention, there is provided a method for producing a synthetic polynucleotide as broadly described above, comprising:

- linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

Preferably, the method further comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in said parent polypeptide sequence. In a preferred embodiment of this type, the fragments are randomly linked together.

Suitably, the method further comprises reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment. In a preferred embodiment of this type, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest. Suitably, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a palindromic sequence or a duplicated sequence) that is refractory to the execution of a task (e.g., cloning or sequencing).

In another aspect, the invention encompasses a computer program product for designing the sequence of a synthetic polypeptide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;

- code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and
  - a computer readable medium that stores the codes.

In yet another aspect, the invention provides a computer program product for designing the sequence of a synthetic polynucleotide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments:
- 10 - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
  - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
    - a computer readable medium that stores the codes.

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In still yet another aspect, the invention provides a computer for designing the sequence of a synthetic polypeptide as broadly described above, wherein said computer comprises:

- 20 (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
- 25 (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.

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In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.

In still yet another aspect, the invention resides in a computer for designing the sequence of a synthetic polynucleotide as broadly described above, wherein said computer comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
- (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.

According to another aspect, the invention contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, together with a pharmaceutically acceptable carrier.

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The composition may optionally comprise an adjuvant.

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In a further aspect, the invention encompasses a method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

According to still a further aspect of the invention, there is provided a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

The invention also encompasses the use of the synthetic polypeptide, the synthetic polynucleotide and the synthetic construct as broadly described above in the study, and modulation of immune responses.

#### **BRIEF DESCRIPTION OF THE DRAWINGS**

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Figure 1 is a diagrammatic representation showing the number of people living with AIDS in 1998 in various parts of the world and most prevalent HIV clades in these regions. Estimates generated by UNAIDS.

Figure 2 is a graphical representation showing trends in the incidence of the common HIV clades and estimates for the future. Graph from the International Aids Vaccine Initiative (IAVI).

Figure 3 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV gag [SEQ ID NO: 1] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV gag protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 4 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV pol [SEQ ID NO: 2] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV pol protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 5 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vif [SEQ ID NO: 3] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vif protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 6 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpr [SEQ ID NO: 4] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpr protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 7 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV tat [SEQ ID NO: 5] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV tat protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 8 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV rev [SEQ ID NO: 6] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV rev protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

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Figure 9 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpu [SEQ ID NO: 7] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpu protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 10 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV env [SEQ ID NO: 8] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade

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consensus sequences for the HIV env protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 11 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV nef [SEQ ID NO: 9] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV nef protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 12 is a diagrammatic representation depicting the systematic segmentation of the designed degenerate consensus sequences for each HIV protein and the reverse translation of each segment into a DNA sequence. Also shown is the number of segments used during random rearrangement and amino acids that were removed. Amino acids surrounded by an open square were removed from the design, because degenerate codons to cater for the desired amino acid combination required too many degenerate bases to comply with the incorporation of degenerate sequence rules outlined in the description of the invention herein. Amino acids surrounded by an open circle were removed only in the segment concerned mainly because they were coded for in an oligonucleotide overlap region. Amino acids marked with an asterisk were designed differently in one fragment compared to the corresponding overlap region (see tat gene)

Figure 13 is a diagrammatic representation showing the first and second most frequently used codons in mammals used to reverse translate HIV protein segments. Also shown are all first and second most frequently used degenerate codons for two amino acids where only one base is varied. Codons used where more than one base was varied were worked out in each case by comparing all the codons for each amino acid. The IUPAC codes for degenerate bases are also shown.

Figure 14 illustrates the construction plan for the HIV Savine showing the approximate sizes of the subcassettes, cassettes and full-length Savine cDNA and the restriction sites involved in joining them together. Also shown are the extra sequences

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added onto each subcassette during their design and a brief description of how the subcassettes, cassettes and full length cDNA were constructed and transferred into appropriate DNA plasmids. Description of full length construction: pA was cleaved with XhoI/SalI and cloned into XhoI arms of the B cassette; pAB was cleaved with XhoI and cloned into XhoI arms of the C cassette; full length construct is excisable with either XbaI/BamHI at the 5' end or BglII at the 3' end. Options for excising cassettes: A) XbaI/BamHI at the 5' end, BglII/XhoI at the 3' end; B) XbaI/BamHI at the 5' end, BglII/SalI at the 3' end. Cleaving plasmid vectors: pDNAVacc is cleavable with XbaI/XhoI (DNA vaccination); pBCB07 or pTK7.5 vectors are cleavable with BamHI/SalI (Recombinant Vaccinia); pAvipox vector pAF09 is cleavable with BamHI/SalI (Recombinant Avipox).

Figure 15 shows the full length DNA (17253 bp) and protein sequence (5742 aas) of the HIV Savine construct. Fragment boundaries are shown, together with the position of each fragment in each designed HIV protein, fragment number (in brackets), spacer residues (two alanine residues) and which fragment the spacer was for (open boxes and arrows). The location of residual restriction site joining sequences corresponding to subcassette or cassette boundaries (shaded boxes) are also shown, along with start and stop codons, Kozak sequence, the location of the murine influenza virus CTL epitope sequence (near the 3' end), important restriction sites at each end and the position of each degenerate amino acid (indicated by 'X').

Figure 16 depicts the layout and position of oligonucleotides in the designed DNA sequence for subcassette A1. The sequences which anneal to the short amplification oligonucleotides are indicated by hatched boxes and the position of oligonucleotide overlap regions are dark shaded.

Figure 17: Panel (a) depicts the stepwise asymmetric PCR of the two halves of subcassette A1 (lanes 2-5 and 7-9, respectively) and final splicing together by SOEing (lane 10). DNA standards in lane 1 are pUC18 digested with Sau3AI. Panel (b) shows the stepwise ligation-mediated joining and PCR amplification of each cassette as indicated. DNA standards in lane 1 are SPP1 cut with EcoRI.

Figure 18: Panel (a) shows summary of the construction of the DNA vaccine plasmids that express one HIV Savine cassette. Panel (b) shows a summary of the

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construction of the plasmids used for marker rescue recombination to generate Vaccinia viruses expressing one HIV Savine cassette. Panel (c) shows a summary of the construction of the DNA vaccine plasmids which each express a version of the full-length HIV Savine cDNA

Figure 19 shows restimulation of HIV specific polyclonal CTL responses from three HIV-infected patients by the HIV Savine constructs. PBMCs from three different patients were restimulated for 7 days by infection with Vaccinia virus pools expressing the HIV Savine cassettes: Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2. The restimulated PBMCs were then mixed with autologous LCLs (effector to target ratio of 50:1), which were either uninfected or infected with either Vaccinia viruses expressing the HIV proteins gag (VV-gag), env (VV-env) or pol (VV-pol), VV-HIV Savine pools 1 (light bars) or 2 (dark bars) or a control Vaccinia virus (VV-Lac) and the amount of <sup>51</sup>Cr released used to determine percent specific lysis. K562 cells were used to determine the level of NK cell-mediated killing in their stimulated culture.

Figure 20 is a diagrammatic representation showing CD4+ proliferation of PBMCs from HIV-1 infected patients restimulated with either Pool1 or Pool2 of the HIV-1 Savine. Briefly PBMCs were stained with CFSE and culture for 6 days with or without VVs encoding either pool1 or pool2 of the HIV-1 Savine. Restimulated Cells were then labelled with antibodies and analysed by FACS.

Figure 21 is a graphical representation showing the CTL response in mice vaccinated with the HIV Savine. C57BL6 mice were immunised with the HIV-1 Savine DNA vaccine comprising the six plasmids described in Figure 18a (100  $\mu$ g total DNA was given as 50  $\mu$ g/leg i.m.). One week later Poxviruses (1x10<sup>7</sup> pfu) comprising Pool 1 of the HIV-1 Savine were used to boost the immune responses. Three weeks later splenocytes from these mice were restimulated with VV-Pool 1 or VV-Pool 2 for 5 days and the resultant effectors used in a <sup>51</sup>Cr release cytotoxicity assay against targets infected with CTRVV, VV-pools or VV expressing the natural antigens from HIV-1.

Figure 22 shows immune responses of HIV Immune Macaques (vaccinated with recombinant FPV expressing gag-pol and challenged with HIV-1 2 years prior to experiment). Monkeys 1 and 2 were immunised once at day 0 with VV Savine pool 1 (Three VVs which together express the entire HIV Savine ). Monkey 3 was immunised

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twice with FPV-gag-pol *i.e.*, Day 0 is 3 weeks after first FPV-gag-pol immunisation. A) IFN-y detection by ELISPOT of whole blood (0.5 mL, venous blood heparinanticoagulated) stimulated with Aldrithiol-2 inactivated whole HIV-1 (20 hours, 20 μg/mL). Plasma samples were then centrifuged (1000xg) and assayed in duplicate for antigen-specific IFN using capture ELISA. B) Flow cytometric detection of HIV-1 specific CD69+/CD8+ T cells. Freshly isolated PBMCs were stimulated with inactivated HIV-1 as above for 16 hours, washed and labelled with the antibodies. Cells were then analysed using a FACScalibur<sup>TM</sup> flow cytometer and data. analysed using Cell-Quest software. C) Flow cytometric detection of HIV-1 specific CD69+/CD4+ T cells carried out as in B).

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Figure 23 shows a diagram of a system used to carry out the instructions encoded by the storage medium of Figures 28 and 29.

Figure 24 depicts a flow diagram showing an embodiment of a method for designing synthetic polynucleotide and synthetic polypeptides of the invention.

Figure 25 shows an algorithm, which *inter alia* utilises the steps of the method shown in Figure 24.

Figure 26 shows an example of applying the algorithm of Figure 25 to an input consensus polyprotein sequence of Hepatitis C 1a to execute the segmentation of the polyprotein sequence, the rearrangement of the segments, the linkage of the rearranged segments and the outputting of synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing Hepatitis C infection.

Figure 27 illustrates an example of applying the algorithm of Figure 25 to input consensus melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to consensus melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1) to facilitate segmentation of those sequences, to rearrange the segments, to link the rearranged segments and to synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing melanoma.

Figure 28 shows a cross section of a magnetic storage medium.

Figure 29 shows a cross section of an optically readable data storage medium.

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Figure 30 shows six HIV Savine cassette sequences (A1 [SEQ ID NO: 393], A2 [SEQ ID NO: 399], B1[SEQ ID NO: 395], B2 [SEQ ID NO: 401], C1 [SEQ ID NO: 397] and C2 [SEQ ID NO: 403]). A1, B1 and C1 can be joined together using, for example, convenient restriction enzyme sites provided at the ends of each cassette to construct an embodiment of a full length HIV Savine [SEQ ID NO: 405]. A2, B2 and C2 can also be joined together to provide another embodiment of a full length HIV Savine with 350 aa mutations common in major HIV clades. The cassettes A/B/C can be joined into single constructs using specific restriction enzyme sites incorporated after the start codon or before the stop codon in the cassettes

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### BRIEF DESCRIPTION OF THE SEQUENCES: SUMMARY TABLE

### TABLE A

SIQUENCE ID NUMBER	SEGUENCE .	LEMGTH
SEQ ID NO: 1	GAG consensus polypeptide	499 aa
SEQ ID NO: 2	POL consensus polypeptide	995 aa
SEQ ID NO: 3	VIF consensus polypeptide	192 aa
SEQ ID NO: 4	VPR consensus polypeptide	96 aa
SEQ ID NO: 5	TAT consensus polypeptide	102 aa
SEQ ID NO: 6	REV consensus polypeptide	123 aa
SEQ ID NO: 7	VPU consensus polypeptide	81 aa
SEQ ID NO: 8	ENV consensus polypeptide	651 aa
SEQ ID NO: 9	NEF consensus polypeptide	206 aa
SEQ ID NO: 10	GAG segment 1	90 nts
SEQ ID NO: 11	Polypeptide encoded by SEQ ID NO: 10	30 aa
SEQ ID NO: 12	GAG segment 2	90 nts
SEQ ID NO: 13	Polypeptide encoded by SEQ ID NO: 12	30 aa
SEQ ID NO: 14	GAG segment 3	90 nts
SEQ ID NO: 15	Polypeptide encoded by SEQ ID NO: 14	30 aa
SEQ ID NO: 16	GAG segment 4	90 nts
SEQ ID NO: 17	Polypeptide encoded by SEQ ID NO: 16	30 aa
SEQ ID NO: 18	GAG segment 5	90 nts
SEQ ID NO: 19	Polypeptide encoded by SEQ ID NO: 18	30 aa
SEQ ID NO: 20	GAG segment 6	90 nts
SEQ ID NO: 21	Polypeptide encoded by SEQ ID NO: 20	30 aa
SEQ ID NO: 22	GAG segment 7	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 23	Polypeptide encoded by SEQ ID NO: 22	30 aa
SEQ ID NO: 24	GAG segment 8	90 nts
SEQ ID NO: 25	Polypeptide encoded by SEQ ID NO: 24	30 aa
SEQ ID NO: 26	GAG segment 9	90 nts
SEQ ID NO: 27	Polypeptide encoded by SEQ ID NO: 26	30 aa
SEQ ID NO: 28	GAG segment 10	90 nts
SEQ ID NO: 29	Polypeptide encoded by SEQ ID NO: 28	30 aa
SEQ ID NO: 30	GAG segment 11	90 nts
SEQ ID NO: 31	Polypeptide encoded by SEQ ID NO: 30	30 aa
SEQ ID NO: 32	GAG segment 12	90 nts
SEQ ID NO: 33	Polypeptide encoded by SEQ ID NO: 32	30 aa
SEQ ID NO: 34	GAG segment 13	90 nts
SEQ ID NO: 35	Polypeptide encoded by SEQ ID NO: 34	30 aa
SEQ ID NO: 36	GAG segment 14	90 nts
SEQ ID NO: 37	Polypeptide encoded by SEQ ID NO: 36	30 aa
SEQ ID NO: 38	GAG segment 15	90 nts
SEQ ID NO: 39	Polypeptide encoded by SEQ ID NO: 38	30 aa
SEQ ID NO: 40	GAG segment 16	90 nts
SEQ ID NO: 41	Polypeptide encoded by SEQ ID NO: 40	30 aa
SEQ ID NO: 42	GAG segment 17	90 nts
SEQ ID NO: 43	Polypeptide encoded by SEQ ID NO: 42	30 aa
SEQ ID NO: 44	GAG segment 18	90 nts
SEQ ID NO: 45	Polypeptide encoded by SEQ ID NO: 44	30 aa
SEQ ID NO: 46	GAG segment 19	90 nts

SEQUENCE ID NUMBER	SEQ TENCE	LENGTH
SEQ ID NO: 47	Polypeptide encoded by SEQ ID NO: 46	30 aa
SEQ ID NO: 48	GAG segment 20	90 nts
SEQ ID NO: 49	Polypeptide encoded by SEQ ID NO: 48	30 aa
SEQ ID NO: 50	GAG segment 21	90 nts
SEQ ID NO: 51	Polypeptide encoded by SEQ ID NO: 50	30 aa
SEQ ID NO: 52	GAG segment 22	90 nts
SEQ ID NO: 53	Polypeptide encoded by SEQ ID NO: 52	30 aa
SEQ ID NO: 54	GAG segment 23	90 nts
SEQ ID NO: 55	Polypeptide encoded by SEQ ID NO: 54	30 aa
SEQ ID NO: 56	GAG segment 24	90 nts
SEQ ID NO: 57	Polypeptide encoded by SEQ ID NO: 56	30 aa
SEQ ID NO: 58	GAG segment 25	90 nts
SEQ ID NO: 59	Polypeptide encoded by SEQ ID NO: 58	30 aa
SEQ ID NO: 60	GAG segment 26	90 nts
SEQ ID NO: 61	Polypeptide encoded by SEQ ID NO: 60	30 aa
SEQ ID NO: 62	GAG segment 27	90 nts
SEQ ID NO: 63	Polypeptide encoded by SEQ ID NO: 62	30 aa
SEQ ID NO: 64	GAG segment 28	90 nts
SEQ ID NO: 65	Polypeptide encoded by SEQ ID NO: 64	30 aa
SEQ ID NO: 66	GAG segment 29	90 nts
SEQ ID NO: 67	Polypeptide encoded by SEQ ID NO: 66	30 aa
SEQ ID NO: 68	GAG segment 30	90 nts
SEQ ID NO: 69	Polypeptide encoded by SEQ ID NO: 68	30 aa
SEQ ID NO: 70	GAG segment 31	90 nts

SIQUENCI III MUMBUR	SEGUENCE	LENGTH
SEQ ID NO: 71	Polypeptide encoded by SEQ ID NO: 70	30 aa
SEQ ID NO: 72	GAG segment 32	90 nts
SEQ ID NO: 73	Polypeptide encoded by SEQ ID NO: 72	30 aa
SEQ ID NO: 74	GAG segment 33	57 nts
SEQ ID NO: 75	Polypeptide encoded by SEQ ID NO: 74	19 aa
SEQ ID NO: 76	POL segment 1	90 nts
SEQ ID NO: 77	Polypeptide encoded by SEQ ID NO: 76	30 aa
SEQ ID NO: 78	POL segment 2	90 nts
SEQ ID NO: 79	Polypeptide encoded by SEQ ID NO: 78	30 aa
SEQ ID NO: 80	POL segment 3	90 nts
SEQ ID NO: 81	Polypeptide encoded by SEQ ID NO: 80	30 aa
SEQ ID NO: 82	POL segment 4	90 nts
SEQ ID NO: 83	Polypeptide encoded by SEQ ID NO: 82	30 aa
SEQ ID NO: 84	POL segment 5	90 nts
SEQ ID NO: 85	Polypeptide encoded by SEQ ID NO: 84	30 aa
SEQ ID NO: 86	POL segment 6	90 nts
SEQ ID NO: 87	Polypeptide encoded by SEQ ID NO: 86	30 aa
SEQ ID NO: 88	POL segment 7	90 nts
SEQ ID NO: 89	Polypeptide encoded by SEQ ID NO: 88	30 aa
SEQ ID NO: 90	POL segment 8	90 nts
SEQ ID NO: 91	Polypeptide encoded by SEQ ID NO: 90	30 aa
SEQ ID NO: 92	POL segment 9	90 nts
SEQ ID NO: 93	Polypeptide encoded by SEQ ID NO: 92	30 aa
SEQ ID NO: 94	POL segment 10	90 nts

SIQUINCI D	TEQUENCE .	LENGTH
NUMBER		
SEQ ID NO: 95	Polypeptide encoded by SEQ ID NO: 94	30 aa
SEQ ID NO: 96	POL segment 11	90 nts
SEQ ID NO: 97	Polypeptide encoded by SEQ ID NO: 96	30 aa
SEQ ID NO: 98	POL segment 12	90 nts
SEQ ID NO: 99	Polypeptide encoded by SEQ ID NO: 98	30 aa
SEQ ID NO: 100	POL segment 13	90 nts
SEQ ID NO: 101	Polypeptide encoded by SEQ ID NO: 100	30 aa
SEQ ID NO: 102	POL segment 14	90 nts
SEQ ID NO: 103	Polypeptide encoded by SEQ ID NO: 102	30 aa
SEQ ID NO: 104	POL segment 15	90 nts
SEQ ID NO: 105	Polypeptide encoded by SEQ ID NO: 104	30 aa
SEQ ID NO: 106	POL segment 16	90 nts
SEQ ID NO: 107	Polypeptide encoded by SEQ ID NO: 106	30 aa
SEQ ID NO: 108	POL segment 17	90 nts
SEQ ID NO: 109	Polypeptide encoded by SEQ ID NO: 108	30 aa
SEQ ID NO: 110	POL segment 18	90 nts
SEQ ID NO: 111	Polypeptide encoded by SEQ ID NO: 110	30 aa
SEQ ID NO: 112	POL segment 19	90 nts
SEQ ID NO: 113	Polypeptide encoded by SEQ ID NO: 112	30 aa
SEQ ID NO: 114	POL segment 20	90 nts
SEQ ID NO: 115	Polypeptide encoded by SEQ ID NO: 114	30 aa
SEQ ID NO: 116	POL segment 21	90 nts
SEQ ID NO: 117	Polypeptide encoded by SEQ ID NO: 116	30 aa
SEQ ID NO: 118	POL segment 22	90 nts

IQVE/CI D	MOLTACE	UENGTH
MUMBER		
SEQ ID NO: 119	Polypeptide encoded by SEQ ID NO: 118	30 aa
SEQ ID NO: 120	POL segment 23	90 nts
SEQ ID NO: 121	Polypeptide encoded by SEQ ID NO: 120	30 aa
SEQ ID NO: 122	POL segment 24	90 nts
SEQ ID NO: 123	Polypeptide encoded by SEQ ID NO: 122	30 aa
SEQ ID NO: 124	POL segment 25	90 nts
SEQ ID NO: 125	Polypeptide encoded by SEQ ID NO: 124	30 aa
SEQ ID NO: 126	POL segment 26	90 nts
SEQ ID NO: 127	Polypeptide encoded by SEQ ID NO: 126	30 aa
SEQ ID NO: 128	POL segment 27	90 nts
SEQ ID NO: 129	Polypeptide encoded by SEQ ID NO: 128	30 aa
SEQ ID NO: 130	POL segment 28	90 nts
SEQ ID NO: 131	Polypeptide encoded by SEQ ID NO: 130	30 aa
SEQ ID NO: 132	POL segment 29	90 nts
SEQ ID NO: 133	Polypeptide encoded by SEQ ID NO: 132	30 aa
SEQ ID NO: 134	POL segment 30	90 nts
SEQ ID NO: 135	Polypeptide encoded by SEQ ID NO: 134	30 aa
SEQ ID NO: 136	POL segment 31	90 nts
SEQ ID NO: 137	Polypeptide encoded by SEQ ID NO: 136	30 aa
SEQ ID NO: 138	POL segment 32	90 nts
SEQ ID NO: 139	Polypeptide encoded by SEQ ID NO: 138	30 aa
SEQ ID NO: 140	POL segment 33	90 nts
SEQ ID NO: 141	Polypeptide encoded by SEQ ID NO: 140	30 aa
SEQ ID NO: 142	POL segment 34	90 nts

LIQUENCI ID MUMBER	iquinci .	IJENGTH
SEQ ID NO: 143	Polypeptide encoded by SEQ ID NO: 142	30 aa
SEQ ID NO: 144	POL segment 35	90 nts
SEQ ID NO: 145	Polypeptide encoded by SEQ ID NO: 144	30 aa
SEQ ID NO: 146	POL segment 36	90 nts
SEQ ID NO: 147	Polypeptide encoded by SEQ ID NO: 146	30 aa
SEQ ID NO: 148	POL segment 37	90 nts
SEQ ID NO: 149	Polypeptide encoded by SEQ ID NO: 148	30 aa
SEQ ID NO: 150	POL segment 38	90 nts
SEQ ID NO: 151	Polypeptide encoded by SEQ ID NO: 150	30 aa
SEQ ID NO: 152	POL segment 39	90 nts
SEQ ID NO: 153	Polypeptide encoded by SEQ ID NO: 152	30 aa
SEQ ID NO: 154	POL segment 40	90 nts
SEQ ID NO: 155	Polypeptide encoded by SEQ ID NO: 154	30 aa
SEQ ID NO: 156	POL segment 41	90 nts
SEQ ID NO: 157	Polypeptide encoded by SEQ ID NO: 156	30 aa
SEQ ID NO: 158	POL segment 42	90 nts
SEQ ID NO: 159	Polypeptide encoded by SEQ ID NO: 158	30 aa
SEQ ID NO: 160	POL segment 43	90 nts
SEQ ID NO: 161	Polypeptide encoded by SEQ ID NO: 160	30 aa
SEQ ID NO: 162	POL segment 44	90 nts
SEQ ID NO: 163	Polypeptide encoded by SEQ ID NO: 162	.30 aa
SEQ ID NO: 164	POL segment 45	90 nts
SEQ ID NO: 165	Polypeptide encoded by SEQ ID NO: 164	30 aa
SEQ ID NO: 166	POL segment 46	90 nts

SEQUENCIM	MOUNCE	LENGTH
NOMBER		
<b>SEQ ID NO: 167</b>	Polypeptide encoded by SEQ ID NO: 166	30 aa
SEQ ID NO: 168	POL segment 47	90 nts
SEQ ID NO: 169	Polypeptide encoded by SEQ ID NO: 168	30 aa
SEQ ID NO: 170	POL segment 48	90 nts
SEQ ID NO: 171	Polypeptide encoded by SEQ ID NO: 170	30 aa
SEQ ID NO: 172	POL segment 49	90 nts
SEQ ID NO: 173	Polypeptide encoded by SEQ ID NO: 172	30 aa
SEQ ID NO: 174	POL segment 50	90 nts
SEQ ID NO: 175	Polypeptide encoded by SEQ ID NO: 174	30 aa
SEQ ID NO: 176	POL segment 51	90 nts
SEQ ID NO: 177	Polypeptide encoded by SEQ ID NO: 176	30 aa
SEQ ID NO: 178	POL segment 52	90 nts
SEQ ID NO: 179	Polypeptide encoded by SEQ ID NO: 178	30 aa
SEQ ID NO: 180	POL segment 53	90 nts
SEQ ID NO: 181	Polypeptide encoded by SEQ ID NO: 180	30 aa
SEQ ID NO: 182	POL segment 54	90 nts
SEQ ID NO: 183	Polypeptide encoded by SEQ ID NO: 182	30 aa
SEQ ID NO: 184	POL segment 55	90 nts
SEQ ID NO: 185	Polypeptide encoded by SEQ ID NO: 184	30 aa
SEQ ID NO: 186	POL segment 56	90 nts
SEQ ID NO: 187	Polypeptide encoded by SEQ ID NO: 186	·30 aa
SEQ ID NO: 188	POL segment 57	90 nts
SEQ ID NO: 189	Polypeptide encoded by SEQ ID NO: 188	30 aa
SEQ ID NO: 190	POL segment 58	90 nts

SIGUINCI ID NUMBER	SEGUENCE	LENGTH
SEQ ID NO: 191	Polypeptide encoded by SEQ ID NO: 190	30 aa
SEQ ID NO: 192	POL segment 59	90 nts
SEQ ID NO: 193	Polypeptide encoded by SEQ ID NO: 192	30 aa
SEQ ID NO: 194	POL segment 60	90 nts
SEQ ID NO: 195	Polypeptide encoded by SEQ ID NO: 194	30 aa
SEQ ID NO: 196	POL segment 61	90 nts
SEQ ID NO: 197	Polypeptide encoded by SEQ ID NO: 196	30 aa
SEQ ID NO: 198	POL segment 62	90 nts
SEQ ID NO: 199	Polypeptide encoded by SEQ ID NO: 198	30 aa
SEQ ID NO: 200	POL segment 63	90 nts
SEQ ID NO: 201	Polypeptide encoded by SEQ ID NO: 200	30 aa
SEQ ID NO: 202	POL segment 64	90 nts
SEQ ID NO: 203	Polypeptide encoded by SEQ ID NO: 202	30 aa
SEQ ID NO: 204	POL segment 65	90 nts
SEQ ID NO: 205	Polypeptide encoded by SEQ ID NO: 204	30 aa
SEQ ID NO: 206	POL segment 66	60 nts
SEQ ID NO: 207	Polypeptide encoded by SEQ ID NO: 206	20 aa <sub>.</sub>
SEQ ID NO: 208	VIF segment 1	90 nts
SEQ ID NO: 209	Polypeptide encoded by SEQ ID NO: 208	30 aa
SEQ ID NO: 210	VIF segment 2	90 nts
SEQ ID NO: 211	Polypeptide encoded by SEQ ID NO: 210	30 aa
SEQ ID NO: 212	VIF segment 3	90 nts
SEQ ID NO: 213	Polypeptide encoded by SEQ ID NO: 212	30 aa
SEQ ID NO: 214	VIF segment 4	90 nts

SEQUENCE (D NUMBER	SEQUENCS.	LENGTH
SEQ ID NO: 215	Polypeptide encoded by SEQ ID NO: 214	30 aa
SEQ ID NO: 216	VIF segment 5	90 nts
SEQ ID NO: 217	Polypeptide encoded by SEQ ID NO: 216	30 aa
SEQ ID NO: 218	VIF segment 6	90 nts
SEQ ID NO: 219	Polypeptide encoded by SEQ ID NO: 218	30 aa
SEQ ID NO: 220	VIF segment 7	90 nts
SEQ ID NO: 221	Polypeptide encoded by SEQ ID NO: 220	30 aa
SEQ ID NO: 222	VIF segment 8	90 nts
SEQ ID NO: 223	Polypeptide encoded by SEQ ID NO: 222	30 aa
SEQ ID NO: 224	VIF segment 9	90 nts
SEQ ID NO: 225	Polypeptide encoded by SEQ ID NO: 224	30 aa
SEQ ID NO: 226	VIF segment 10	90 nts
SEQ ID NO: 227	Polypeptide encoded by SEQ ID NO: 226	30 aa
SEQ ID NO: 228	VIF segment 11	90 nts
SEQ ID NO: 229	Polypeptide encoded by SEQ ID NO: 228	30 aa
SEQ ID NO: 230	VIF segment 12	81 nts
SEQ ID NO: 231	Polypeptide encoded by SEQ ID NO: 230	27 aa
SEQ ID NO: 232	VPR segment 1	90 nts
SEQ ID NO: 233	Polypeptide encoded by SEQ ID NO: 232	30 aa
SEQ ID NO: 234	VPR segment 2	90 nts
SEQ ID NO: 235	Polypeptide encoded by SEQ ID NO: 234	30 aa
SEQ ID NO: 236	VPR segment 3	90 nts
SEQ ID NO: 237	Polypeptide encoded by SEQ ID NO: 236	30 aa
SEQ ID NO: 238	VPR segment 4	90 nts

SIGUENCI (D) NUMBER	SEQUENCE.	LEMGTH
SEQ ID NO: 239	Polypeptide encoded by SEQ ID NO: 238	30 aa
SEQ ID NO: 240	VPR segment 5	90 nts
SEQ ID NO: 241	Polypeptide encoded by SEQ ID NO: 240	30 aa
SEQ ID NO: 242	VPR segment 6	63 nts
SEQ ID NO: 243	Polypeptide encoded by SEQ ID NO: 242	21 aa
SEQ ID NO: 244	TAT segment 1	90 nts
SEQ ID NO: 245	Polypeptide encoded by SEQ ID NO: 244	30 aa
SEQ ID NO: 246	TAT segment 2	90 nts
SEQ ID NO: 247	Polypeptide encoded by SEQ ID NO: 246	30 aa
SEQ ID NO: 248	TAT segment 3	90 nts
SEQ ID NO: 249	Polypeptide encoded by SEQ ID NO: 248	30 aa
SEQ ID NO: 250	TAT segment 4	90 nts
SEQ ID NO: 251	Polypeptide encoded by SEQ ID NO: 250	30 aa
SEQ ID NO: 252	TAT segment 5	90 nts
<b>SEQ ID NO: 253</b>	Polypeptide encoded by SEQ ID NO: 252	30 aa
SEQ ID NO: 254	TAT segment 6	81 nts
<b>SEQ ID NO: 255</b>	Polypeptide encoded by SEQ ID NO: 254	27 aa
SEQ ID NO: 256	REV segment 1	90 nts
<b>SEQ ID NO: 257</b>	Polypeptide encoded by SEQ ID NO: 256	30 aa
<b>SEQ ID NO: 258</b>	REV segment 2	90 nts
SEQ ID NO: 259	Polypeptide encoded by SEQ ID NO: 258	30 aa
SEQ ID NO: 260	REV segment 3	90 nts
SEQ ID NO: 261	Polypeptide encoded by SEQ ID NO: 260	30 aa
SEQ ID NO: 262	REV segment 4	90 nts

MONTHED MONTHER		LLMGTH
SEQ ID NO: 263	Polypeptide encoded by SEQ ID NO: 262	30 aa
SEQ ID NO: 264	REV segment 5	90 nts
SEQ ID NO: 265	Polypeptide encoded by SEQ ID NO: 264	30 aa
SEQ ID NO: 266	REV segment 6	90 nts
SEQ ID NO: 267	Polypeptide encoded by SEQ ID NO: 266	30 aa
SEQ ID NO: 268	REV segment 7	90 nts
SEQ ID NO: 269	Polypeptide encoded by SEQ ID NO: 268	30 aa
SEQ ID NO: 270	REV segment 8	54 nts
SEQ ID NO: 271	Polypeptide encoded by SEQ ID NO: 270	18 aa
SEQ ID NO: 272	VPU segment 1	90 nts
SEQ ID NO: 273	Polypeptide encoded by SEQ ID NO: 272	30 aa
SEQ ID NO: 274	VPU segment 2	90 nts
SEQ ID NO: 275	Polypeptide encoded by SEQ ID NO: 274	30 aa
SEQ ID NO: 276	VPU segment 3	90 nts
SEQ ID NO: 277	Polypeptide encoded by SEQ ID NO: 276	30 aa
SEQ ID NO: 278	VPU segment 4	90 nts
SEQ ID NO: 279	Polypeptide encoded by SEQ ID NO: 278	30 aa
SEQ ID NO: 280	VPU segment 5	63 nts
SEQ ID NO: 281	Polypeptide encoded by SEQ ID NO: 280	21 aa
SEQ ID NO: 282	ENV segment 1	90 nts
SEQ ID NO: 283	Polypeptide encoded by SEQ ID NO: 282	30 aa
SEQ ID NO: 284	ENV segment 2	90 nts
SEQ ID NO: 285	Polypeptide encoded by SEQ ID NO: 284	30 aa
SEQ ID NO: 286	ENV segment 3	90 nts

SIQUENCE ID MUMBER	SIQUENCE	LENGTH
SEQ ID NO: 287	Polypeptide encoded by SEQ ID NO: 286	30 aa
SEQ ID NO: 288	ENV segment 4	90 nts
SEQ ID NO: 289	Polypeptide encoded by SEQ ID NO: 288	30 aa
SEQ ID NO: 290	ENV segment 5	90 nts
SEQ ID NO: 291	Polypeptide encoded by SEQ ID NO: 290	30 aa
SEQ ID NO: 292	ENV segment 6	90 nts
SEQ ID NO: 293	Polypeptide encoded by SEQ ID NO: 292	30 aa
SEQ ID NO: 294	ENV segment 7	90 nts
SEQ ID NO: 295	Polypeptide encoded by SEQ ID NO: 294	30 aa
SEQ ID NO: 296	ENV segment 8	90 nts
SEQ ID NO: 297	Polypeptide encoded by SEQ ID NO: 296	30 aa
SEQ ID NO: 298	ENV segment 9	57 nts
SEQ ID NO: 299	Polypeptide encoded by SEQ ID NO: 298	19 aa
SEQ ID NO: 300	GAP A segment 1	90 nts
SEQ ID NO: 301	Polypeptide encoded by SEQ ID NO: 300	30 aa
SEQ ID NO: 302	GAP A segment 2	90 nts
SEQ ID NO: 303	Polypeptide encoded by SEQ ID NO: 302	30 aa
SEQ ID NO: 304	GAP A segment 3	90 nts
SEQ ID NO: 305	Polypeptide encoded by SEQ ID NO: 304	30 aa
SEQ ID NO: 306	GAP A segment 4	90 nts
<b>SEQ ID NO: 307</b>	Polypeptide encoded by SEQ ID NO: 306	30 aa
<b>SEQ ID NO: 308</b>	GAP A segment 5	90 nts
SEQ ID NO: 309	Polypeptide encoded by SEQ ID NO: 308	30 aa
SEQ ID NO: 310	GAP A segment 6	90 nts

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SEQUENCE ID MU-BER	SIQUENCI 8	LENGTH
SEQ ID NO: 311	Polypeptide encoded by SEQ ID NO: 310	30 aa
SEQ ID NO: 312	GAP A segment 7	75 nts
SEQ ID NO: 313	Polypeptide encoded by SEQ ID NO: 312	25 nts
SEQ ID NO: 314	GAP B segment 1	90 nts
SEQ ID NO: 315	Polypeptide encoded by SEQ ID NO: 314	30 aa
SEQ ID NO: 316	GAP B segment 2	90 nts
SEQ ID NO: 317	Polypeptide encoded by SEQ ID NO: 316	30 aa
SEQ ID NO: 318	GAP B segment 3	90 nts
SEQ ID NO: 319	Polypeptide encoded by SEQ ID NO: 318	30 aa
SEQ ID NO: 320	GAP B segment 4	90 nts
SEQ ID NO: 321	Polypeptide encoded by SEQ ID NO: 320	30 aa
SEQ ID NO: 322	GAP B segment 5	90 nts
SEQ ID NO: 323	Polypeptide encoded by SEQ ID NO: 322	30 aa
SEQ ID NO: 324	GAP B segment 6	90 nts
SEQ ID NO: 325	Polypeptide encoded by SEQ ID NO: 324	30 aa
SEQ ID NO: 326	GAP B segment 7	90 nts
SEQ ID NO: 327	Polypeptide encoded by SEQ ID NO: 326	30 aa
SEQ ID NO: 328	GAP B segment 8 .	90 nts
SEQ ID NO: 329	Polypeptide encoded by SEQ ID NO: 328	30 aa
SEQ ID NO: 330	GAP B segment 9	90 nts
<b>SEQ ID NO: 331</b>	Polypeptide encoded by SEQ ID NO: 330	30 aa
SEQ ID NO: 332	GAP B segment 10	90 nts
SEQ ID NO: 333	Polypeptide encoded by SEQ ID NO: 332	30 aa
SEQ ID NO: 334	GAP B segment 11	90 nts

SEGUENCE ED NUMBER	SIGCENCI	LENGTH
SEQ ID NO: 335	Polypeptide encoded by SEQ ID NO: 334	30 aa
SEQ ID NO: 336	GAP B segment 12	90 nts .
SEQ ID NO: 337	Polypeptide encoded by SEQ ID NO: 336	30 aa
SEQ ID NO: 338	GAP B segment 13	90 nts
SEQ ID NO: 339	Polypeptide encoded by SEQ ID NO: 338	30 aa
SEQ ID NO: 340	GAP B segment 14	90 nts
SEQ ID NO: 341	Polypeptide encoded by SEQ ID NO: 340	30 aa
SEQ ID NO: 342	GAP B segment 15	90 nts
SEQ ID NO: 343	Polypeptide encoded by SEQ ID NO: 342	30 aa
SEQ ID NO: 344	GAP B segment 16	90 nts
SEQ ID NO: 345	Polypeptide encoded by SEQ ID NO: 344	30 aa
SEQ ID NO: 346	GAP B segment 17	90 nts
SEQ ID NO: 347	Polypeptide encoded by SEQ ID NO: 346	30 aa
SEQ ID NO: 348	GAP B segment 18	90 nts
SEQ ID NO: 349	Polypeptide encoded by SEQ ID NO: 348	30 aa
SEQ ID NO: 350	GAP B segment 19	90 nts
SEQ ID NO: 351	Polypeptide encoded by SEQ ID NO: 350	30 aa
SEQ ID NO: 352	GAP B segment 20	90 nts
SEQ ID NO: 353	Polypeptide encoded by SEQ ID NO: 352	30 aa
SEQ ID NO: 354	GAP B segment 21	90 nts
SEQ ID NO: 355	Polypeptide encoded by SEQ ID NO: 354	30 aa
SEQ ID NO: 356	GAP B segment 22	90 nts
SEQ ID NO: 357	Polypeptide encoded by SEQ ID NO: 356	30 aa
SEQ ID NO: 358	GAP B segment 23	90 nts

SEQUENCE ID NUMBER	SEÇCENCE	LENGTH
SEQ ID NO: 359	Polypeptide encoded by SEQ ID NO: 358	30 aa
SEQ ID NO: 360	GAP B segment 24	90 nts
SEQ ID NO: 361	Polypeptide encoded by SEQ ID NO: 360	30 aa
SEQ ID NO: 362	GAP B segment 25	90 nts
SEQ ID NO: 363	Polypeptide encoded by SEQ ID NO: 362	30 aa
SEQ ID NO: 364	GAP B segment 26	66 nts
SEQ ID NO: 365	Polypeptide encoded by SEQ ID NO: 364	22 aa
SEQ ID NO: 366	NEF segment 1	90 nts
SEQ ID NO: 367	Polypeptide encoded by SEQ ID NO: 366	30 aa
SEQ ID NO: 368	NEF segment 2	90 nts
SEQ ID NO: 369	Polypeptide encoded by SEQ ID NO: 368	30 aa
SEQ ID NO: 370	NEF segment 3	90 nts
SEQ ID NO: 371	Polypeptide encoded by SEQ ID NO: 370	30 aa
SEQ ID NO: 372	NEF segment 4	90 nts
SEQ ID NO: 373	Polypeptide encoded by SEQ ID NO: 372	30 aa
SEQ ID NO: 374	NEF segment 5	90 nts
SEQ ID NO: 375	Polypeptide encoded by SEQ ID NO: 374	30 aa
SEQ ID NO: 376	NEF segment 6	90 nts
SEQ ID NO: 377	Polypeptide encoded by SEQ ID NO: 376	30 aa
SEQ ID NO: 378	NEF segment 7	90 nts
SEQ ID NO: 379	Polypeptide encoded by SEQ ID NO: 378	30 aa
SEQ ID NO: 380	NEF segment 8	90 nts
SEQ ID NO: 381	Polypeptide encoded by SEQ ID NO: 380	30 aa
SEQ ID NO: 382	NEF segment 9	90 nts

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SEQUENCI DO MUNBER	SEQUENCE	LENGTH
SEQ ID NO: 383	Polypeptide encoded by SEQ ID NO: 382	30 aa
SEQ ID NO: 384	NEF segment 10	90 nts
SEQ ID NO: 385	Polypeptide encoded by SEQ ID NO: 384	30 aa
SEQ ID NO: 386	NEF segment 11	90 nts
SEQ ID NO: 387	Polypeptide encoded by SEQ ID NO: 386	30 aa
SEQ ID NO: 388	NEF segment 12	90 nts
SEQ ID NO: 389	Polypeptide encoded by SEQ ID NO: 388	30 aa
SEQ ID NO: 390	NEF segment 13	78 nts
SEQ ID NO: 391	Polypeptide encoded by SEQ ID NO: 390	26 aa
SEQ ID NO: 392	HIV Cassette A1	5703 nts
SEQ ID NO: 393	Polypeptide encoded by SEQ ID NO:392	1896 aa
SEQ ID NO: 394	HIV Cassette B1	5685 nts
SEQ ID NO: 395	Polypeptide encoded by SEQ ID NO: 394	1890 aa
SEQ ID NO: 396	HIV Cassette C1	5925 nts
SEQ ID NO: 397	Polypeptide encoded by SEQ ID NO: 396	1967 aa
SEQ ID NO: 398	HIV Cassette A2	5703 nts
SEQ ID NO: 399	Polypeptide encoded by SEQ ID NO: 398	1896 aa
SEQ ID NO: 400	HIV Cassette B2	5685 nts
SEQ ID NO: 401	Polypeptide encoded by SEQ ID NO: 400	1890 aa
SEQ ID NO: 402	HIV Cassette C2	5925 nts
SEQ ID NO: 403	Polypeptide encoded by SEQ ID NO: 402	1967 aa
SEQ ID NO: 404	HIV complete Savine	17244 nts
SEQ ID NO: 405	Polypeptide encoded by SEQ ID NO: 404	5747 aa
SEQ ID NO: 406	HepC1a consensus polyprotein sequence	3011 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 407	HepCla segment 1	90 nts
SEQ ID NO: 408	Polypeptide encoded by SEQ ID NO: 407	30 aa
SEQ ID NO: 409	HepC1a segment 2	90 nts
SEQ ID NO: 410	Polypeptide encoded by SEQ ID NO: 409	30 aa
SEQ ID NO: 411	HepCla segment 3	90 nts
SEQ ID NO: 412	Polypeptide encoded by SEQ ID NO: 411	30 aa
SEQ ID NO: 413	HepC1a segment 4	90 nts
SEQ ID NO: 414	Polypeptide encoded by SEQ ID NO: 413	30 aa
SEQ ID NO: 415	HepCla segment 5	90 nts
SEQ ID NO: 416	Polypeptide encoded by SEQ ID NO: 415	30 aa
SEQ ID NO: 417	HepCla segment 6	90 nts
SEQ ID NO: 418	Polypeptide encoded by SEQ ID NO: 417	30 aa
SEQ ID NO: 419	HepCla segment 7	90 nts
SEQ ID NO: 420	Polypeptide encoded by SEQ ID NO: 419	30 aa
SEQ ID NO: 421	HepCla segment 8	90 nts
SEQ ID NO: 422	Polypeptide encoded by SEQ ID NO: 421	30 aa
SEQ ID NO: 423	HepCla segment 9	90 nts
SEQ ID NO: 424	Polypeptide encoded by SEQ ID NO: 423	30 aa
SEQ ID NO: 425	HepCla segment 10	90 nts
SEQ ID NO: 426	Polypeptide encoded by SEQ ID NO: 425	30 aa
SEQ ID NO: 427	HepCla segment 11	90 nts
SEQ ID NO: 428	Polypeptide encoded by SEQ ID NO: 427	30 aa
SEQ ID NO: 429	HepCla segment 12	90 nts
SEQ ID NO: 430	Polypeptide encoded by SEQ ID NO: 429	30 aa

SIGUENCI ID NUMBER	NIQUINCI	LENGTH
SEQ ID NO: 431	HepCla segment 13	90 nts
SEQ ID NO: 432	Polypeptide encoded by SEQ ID NO: 431	30 aa
SEQ ID NO: 433	HepCla segment 14	90 nts
SEQ ID NO: 434	Polypeptide encoded by SEQ ID NO: 433	30 aa
SEQ ID NO: 435	HepC1a segment 15	90 nts
SEQ ID NO: 436	Polypeptide encoded by SEQ ID NO: 435	30 aa
SEQ ID NO: 437	HepCla segment 16	90 nts
SEQ ID NO: 438	Polypeptide encoded by SEQ ID NO: 437	30 aa
SEQ ID NO: 439	HepC1a segment 17	90 nts
SEQ ID NO: 440	Polypeptide encoded by SEQ ID NO: 439	30 aa
SEQ ID NO: 441	HepCla segment 18	90 nts
SEQ ID NO: 442	Polypeptide encoded by SEQ ID NO: 441	30 aa
SEQ ID NO: 443	HepCla segment 19	90 nts
SEQ ID NO: 444	Polypeptide encoded by SEQ ID NO: 443	30 aa
SEQ ID NO: 445	HepCla segment 20	90 nts
SEQ ID NO: 446	Polypeptide encoded by SEQ ID NO: 445	30 aa
SEQ ID NO: 447	HepCla segment 21	90 nts
SEQ ID NO: 448	Polypeptide encoded by SEQ ID NO: 447	30 aa
SEQ ID NO: 449	HepC1a segment 22	90 nts
SEQ ID NO: 450	Polypeptide encoded by SEQ ID NO: 449	30 aa
SEQ ID NO: 451	HepC1a segment 23	90 nts
SEQ ID NO: 452	Polypeptide encoded by SEQ ID NO: 451	30 aa
SEQ ID NO: 453	HepCla segment 24	90 nts
SEQ ID NO: 454	Polypeptide encoded by SEQ ID NO: 453	30 aa

SEQUENCE ID NUMBER	EQUAL CE	LENGTH
SEQ ID NO: 455	HepCla segment 25	90 nts
SEQ ID NO: 456	Polypeptide encoded by SEQ ID NO: 455	30 aa
SEQ ID NO: 457	HepCla segment 26	90 nts
SEQ ID NO: 458	Polypeptide encoded by SEQ ID NO: 457	30 aa
SEQ ID NO: 459	HepCla segment 27	90 nts
SEQ ID NO: 460	Polypeptide encoded by SEQ ID NO: 459	30 aa
SEQ ID NO: 461	HepC1a segment 28	90 nts
SEQ ID NO: 462	Polypeptide encoded by SEQ ID NO: 461	30 aa
SEQ ID NO: 463	HepC1a segment 29	90 nts
SEQ ID NO: 464	Polypeptide encoded by SEQ ID NO: 463	30 aa
SEQ ID NO: 465	HepC1a segment 30	90 nts
SEQ ID NO: 466	Polypeptide encoded by SEQ ID NO: 465	30 aa
SEQ ID NO: 467	HepCla segment 31	90 nts
SEQ ID NO: 468	Polypeptide encoded by SEQ ID NO: 467	30 aa
SEQ ID NO: 469	HepCla segment 32	90 nts
SEQ ID NO: 470	Polypeptide encoded by SEQ ID NO: 469	30 aa
SEQ ID NO: 471	HepC1a segment 33	90 nts
SEQ ID NO: 472	Polypeptide encoded by SEQ ID NO: 471	30 aa
SEQ ID NO: 473	HepCla segment 34	90 nts
SEQ ID NO: 474	Polypeptide encoded by SEQ ID NO: 473	30 aa
SEQ ID NO: 475	HepC1a segment 35	90 nts
SEQ ID NO: 476	Polypeptide encoded by SEQ ID NO: 475	30 aa
SEQ ID NO: 477	HepCla segment 36	90 nts
SEQ ID NO: 478	Polypeptide encoded by SEQ ID NO: 477	30 aa

SEQUENCI ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 479	HepCla segment 37	90 nts
SEQ ID NO: 480	Polypeptide encoded by SEQ ID NO: 479	30 aa
SEQ ID NO: 481	HepCla segment 38	90 nts
SEQ ID NO: 482	Polypeptide encoded by SEQ ID NO: 481	30 aa
SEQ ID NO: 483	HepC1a segment 39	90 nts
SEQ ID NO: 484	Polypeptide encoded by SEQ ID NO: 483	30 aa
SEQ ID NO: 485	HepCla segment 40	90 nts
SEQ ID NO: 486	Polypeptide encoded by SEQ ID NO: 485	30 aa
SEQ ID NO: 487	HepC1a segment 41	90 nts
SEQ ID NO: 488	Polypeptide encoded by SEQ ID NO: 487	,30 aa
SEQ ID NO: 489	HepC1a segment 42	90 nts
SEQ ID NO: 490	Polypeptide encoded by SEQ ID NO: 489	30 aa
SEQ ID NO: 491	HepC1a segment 43	90 nts
SEQ ID NO: 492	Polypeptide encoded by SEQ ID NO: 491	30 aa
SEQ ID NO: 493	HepCla segment 44	90 nts
SEQ ID NO: 494	Polypeptide encoded by SEQ ID NO: 493	30 aa
SEQ ID NO: 495	HepCla segment 45	90 nts
SEQ ID NO: 496	Polypeptide encoded by SEQ ID NO: 495	30 aa
SEQ ID NO: 497	HepC1a segment 46	90 nts
SEQ ID NO: 498	Polypeptide encoded by SEQ ID NO: 497	30 aa
SEQ ID NO: 499	HepCla segment 47	90 nts
SEQ ID NO: 500	Polypeptide encoded by SEQ ID NO: 499	30 aa
SEQ ID NO: 501	HepCla segment 48	90 nts
SEQ ID NO: 502	Polypeptide encoded by SEQ ID NO: 501	30 aa

SEQUENCI ID NUMBER	SEQUENCS	LENGTH
SEQ ID NO: 503	HepCla segment 49	90 nts
SEQ ID NO: 504	Polypeptide encoded by SEQ ID NO: 503	30 aa
SEQ ID NO: 505	HepC1a segment 50	90 nts
SEQ ID NO: 506	Polypeptide encoded by SEQ ID NO: 505	30 aa
SEQ ID NO: 507	HepCla segment 51	90 nts
SEQ ID NO: 508	Polypeptide encoded by SEQ ID NO: 507	30 aa
SEQ ID NO: 509	HepCla segment 52	.90 nts
SEQ ID NO: 510	Polypeptide encoded by SEQ ID NO: 509	30 aa
SEQ ID NO: 511	HepC1a segment 53	90 nts
SEQ ID NO: 512	Polypeptide encoded by SEQ ID NO: 511	30 aa
SEQ ID NO: 513	HepC1a segment 54	90 nts
SEQ ID NO: 514	Polypeptide encoded by SEQ ID NO: 513	30 aa
SEQ ID NO: 515	HepC1a segment 55	90 nts
SEQ ID NO: 516	Polypeptide encoded by SEQ ID NO: 515	30 aa
SEQ ID NO: 517	HepCla segment 56	90 nts
SEQ ID NO: 518	Polypeptide encoded by SEQ ID NO: 517	30 aa
SEQ ID NO: 519	HepC1a segment 57	90 nts
SEQ ID NO: 520	Polypeptide encoded by SEQ ID NO: 519	30 aa
SEQ ID NO: 521	HepCla segment 58	90 nts
SEQ ID NO: 522	Polypeptide encoded by SEQ ID NO: 521	30 aa
SEQ ID NO: 523	HepCla segment 59	90 nts
SEQ ID NO: 524	Polypeptide encoded by SEQ ID NO: 523	30 aa
SEQ ID NO: 525	HepC1a segment 60	90 nts
SEQ ID NO: 526	Polypeptide encoded by SEQ ID NO: 525	30 aa

SEQUENCE ID NUMBER	SIQUENCE	LENGTH
SEQ ID NO: 527	HepC1a segment 61	90 nts
SEQ ID NO: 528	Polypeptide encoded by SEQ ID NO: 527	30 aa
SEQ ID NO: 529	HepC1a segment 62	90 nts
SEQ ID NO: 530	Polypeptide encoded by SEQ ID NO: 529	30 aa
SEQ ID NO: 531	HepC1a segment 63	90 nts
SEQ ID NO: 532	Polypeptide encoded by SEQ ID NO: 531	30 aa
SEQ ID NO: 533	HepC1a segment 64	90 nts
SEQ ID NO: 534	Polypeptide encoded by SEQ ID NO: 533	30 aa
SEQ ID NO: 535	HepC1a segment 65	90 nts
SEQ ID NO: 536	Polypeptide encoded by SEQ ID NO: 535	30 aa
SEQ ID NO: 537	HepCla segment 66	90 nts
SEQ ID NO: 538	Polypeptide encoded by SEQ ID NO: 537	30 aa
SEQ ID NO: 539	HepCla segment 67	90 nts
SEQ ID NO: 540	Polypeptide encoded by SEQ ID NO: 539	30 aa
SEQ ID NO: 541	HepCla segment 68	90 nts
SEQ ID NO: 542	Polypeptide encoded by SEQ ID NO: 541	30 aa
SEQ ID NO: 543	HepCla segment 69	90 nts
SEQ ID NO: 544	Polypeptide encoded by SEQ ID NO: 543	30 aa
SEQ ID NO: 545	HepCla segment 70	90 nts
SEQ ID NO: 546	Polypeptide encoded by SEQ ID NO:545	30 aa
SEQ ID NO: 547	HepCla segment 71	90 nts
SEQ ID NO: 548	Polypeptide encoded by SEQ ID NO: 547	30 aa
SEQ ID NO: 549	HepCla segment 72	90 nts
SEQ ID NO: 550	Polypeptide encoded by SEQ ID NO: 549	30 aa

SEQUENCE D NUABER	SEQUENCE	LENGTH
SEQ ID NO: 551	HepC1a segment 73	90 nts
SEQ ID NO: 552	Polypeptide encoded by SEQ ID NO: 551	30 aa
SEQ ID NO: 553	HepCla segment 74	90 nts
SEQ ID NO: 554	Polypeptide encoded by SEQ ID NO: 553	30 aa
SEQ ID NO: 555	HepC1a segment 75	90 nts
SEQ ID NO: 556	Polypeptide encoded by SEQ ID NO: 555	30 aa
SEQ ID NO: 557	HepCla segment 76	90 nts
SEQ ID NO: 558	Polypeptide encoded by SEQ ID NO: 557	30 aa
SEQ ID NO: 559	HepCla segment 77	90 nts
SEQ ID NO: 560	Polypeptide encoded by SEQ ID NO: 559	30 aa
SEQ ID NO: 561	HepCla segment 78	90 nts
SEQ ID NO: 562	Polypeptide encoded by SEQ ID NO: 561	30 aa
SEQ ID NO: 563	HepCla segment 79	90 nts
SEQ ID NO: 564	Polypeptide encoded by SEQ ID NO: 563	30 aa
SEQ ID NO: 565	HepCla segment 80	90 nts
SEQ ID NO: 566	Polypeptide encoded by SEQ ID NO: 565	30 aa
SEQ ID NO: 567	HepCla segment 81	90 nts
SEQ ID NO: 568	Polypeptide encoded by SEQ ID NO: 567	30 aa
SEQ ID NO: 569	HepCla segment 82	90 nts
SEQ ID NO: 570	Polypeptide encoded by SEQ ID NO: 569	30 aa
SEQ ID NO: 571	HepCla segment 83	90 nts
SEQ ID NO: 572	Polypeptide encoded by SEQ ID NO: 571	30 aa
SEQ ID NO: 573	HepCla segment 84	90 nts
SEQ ID NO: 574	Polypeptide encoded by SEQ ID NO: 573	30 aa

SIQUENCI 10 NUMBER	IBQUENCS	LENGTH
SEQ ID NO: 575	HepCla segment 85	90 nts
SEQ ID NO: 576	Polypeptide encoded by SEQ ID NO: 575	30 aa
SEQ ID NO: 577	HepC1a segment 86	90 nts
SEQ ID NO: 578	Polypeptide encoded by SEQ ID NO: 577	30 aa
SEQ ID NO: 579	HepCla segment 87	90 nts
SEQ ID NO: 580	Polypeptide encoded by SEQ ID NO: 579	30 aa
SEQ ID NO: 581	HepCla segment 88	90 nts
SEQ ID NO: 582	Polypeptide encoded by SEQ ID NO: 581	30 aa
SEQ ID NO: 583	HepCla segment 89	90 nts
SEQ ID NO: 584	Polypeptide encoded by SEQ ID NO: 583	30 aa
SEQ ID NO: 585	HepC1a segment 90	90 nts
SEQ ID NO: 586	Polypeptide encoded by SEQ ID NO: 585	30 aa
SEQ ID NO: 587	HepC1a segment 91	90 nts
SEQ ID NO: 588	Polypeptide encoded by SEQ ID NO: 587	30 aa
SEQ ID NO: 589	HepC1a segment 92	90 nts
SEQ ID NO: 590	Polypeptide encoded by SEQ ID NO: 589	30 aa
SEQ ID NO: 591	HepC1a segment 93	90 nts
SEQ ID NO: 592	Polypeptide encoded by SEQ ID NO: 591	30 aa
SEQ ID NO: 593	HepC1a segment 94	90 nts
SEQ ID NO: 594	Polypeptide encoded by SEQ ID NO: 593	30 aa
SEQ ID NO: 595	HepCla segment 95	90 nts
SEQ ID NO: 596	Polypeptide encoded by SEQ ID NO: 595	30 aa
SEQ ID NO: 597	HepCla segment 96	90 nts
SEQ ID NO: 598	Polypeptide encoded by SEQ ID NO: 597	30 aa

SEQUENCE AD NUMBER	SEQUENCE :	Lingth
SEQ ID NO: 599	HepCla segment 97	90 nts
SEQ ID NO: 600	Polypeptide encoded by SEQ ID NO: 599	30 aa
SEQ ID NO: 601	HepC1a segment 98	90 nts
SEQ ID NO: 602	Polypeptide encoded by SEQ ID NO: 601	30 aa
SEQ ID NO: 603	HepCla segment 99	90 nts
SEQ ID NO: 604	Polypeptide encoded by SEQ ID NO: 603	30 aa
SEQ ID NO: 605	HepC1a segment 100	90 nts
SEQ ID NO: 606	Polypeptide encoded by SEQ ID NO: 605	30 aa
SEQ ID NO: 607	HepC1a segment 101	90 nts
SEQ ID NO: 608	Polypeptide encoded by SEQ ID NO: 607	30 aa
SEQ ID NO: 609	HepC1a segment 102	90 nts
SEQ ID NO: 610	Polypeptide encoded by SEQ ID NO: 609	30 aa
SEQ ID NO: 611	HepC1a segment 103	90 nts
SEQ ID NO: 612	Polypeptide encoded by SEQ ID NO: 611	30 aa
SEQ ID NO: 613	HepCla segment 104	90 nts
SEQ ID NO: 614	Polypeptide encoded by SEQ ID NO: 613	30 aa
SEQ ID NO: 615	HepCla segment 105	90 nts
SEQ ID NO: 616	Polypeptide encoded by SEQ ID NO: 615	30 aa
SEQ ID NO: 617	HepC1a segment 106	90 nts
SEQ ID NO: 618	Polypeptide encoded by SEQ ID NO: 617	30 aa
SEQ ID NO: 619	HepCla segment 107	90 nts
SEQ ID NO: 620	Polypeptide encoded by SEQ ID NO: 619	30 aa
SEQ ID NO: 621	HepCla segment 108	90 nts
SEQ ID NO: 622	Polypeptide encoded by SEQ ID NO: 621	30 aa

SEQUENCE DO NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 623	HepCla segment 109	90 nts
SEQ ID NO: 624	Polypeptide encoded by SEQ ID NO: 623	30 aa
SEQ ID NO: 625	HepCla segment 110	90 nts
SEQ ID NO: 626	Polypeptide encoded by SEQ ID NO: 625	30 aa
SEQ ID NO: 627	HepCla segment 111	90 nts
SEQ ID NO: 628	Polypeptide encoded by SEQ ID NO: 627	30 aa
SEQ ID NO: 629	HepC1a segment 112	90 nts
SEQ ID NO: 630	Polypeptide encoded by SEQ ID NO: 629	30 aa
SEQ ID NO: 631	HepC1a segment 113	90 nts
SEQ ID NO: 632	Polypeptide encoded by SEQ ID NO: 631	30 aa
SEQ ID NO: 633	HepCla segment 114	90 nts
SEQ ID NO: 634	Polypeptide encoded by SEQ ID NO: 633	30 aa
SEQ ID NO: 635	HepCla segment 115	90 nts
SEQ ID NO: 636	Polypeptide encoded by SEQ ID NO: 635	30 aa
SEQ ID NO: 637	HepCla segment 116	90 nts
SEQ ID NO: 638	Polypeptide encoded by SEQ ID NO: 637	30 aa
SEQ ID NO: 639	HepCla segment 117	90 nts
SEQ ID NO: 640	Polypeptide encoded by SEQ ID NO: 639	30 aa
SEQ ID NO: 641	HepCla segment 118	90 nts
SEQ ID NO: 642	Polypeptide encoded by SEQ ID NO: 641	30 aa
SEQ ID NO: 643	HepCla segment 119	.90 nts
SEQ ID NO: 644	Polypeptide encoded by SEQ ID NO: 643	30 aa
SEQ ID NO: 645	HepC1a segment 120	90 nts
SEQ ID NO: 646	Polypeptide encoded by SEQ ID NO: 645	30 aa

SEGUENCE D NUMBER	SAQUENCE	LENGTH
SEQ ID NO: 647	HepCla segment 121	90 nts
SEQ ID NO: 648	Polypeptide encoded by SEQ ID NO: 647	30 aa
SEQ ID NO: 649	HepC1a segment 122	90 nts
SEQ ID NO: 650	Polypeptide encoded by SEQ ID NO: 649	30 aa
SEQ ID NO: 651	HepC1a segment 123	90 nts
SEQ ID NO: 652	Polypeptide encoded by SEQ ID NO: 651	30 aa
SEQ ID NO: 653	HepC1a segment 124	90 nts
SEQ ID NO: 654	Polypeptide encoded by SEQ ID NO: 653	30 aa
SEQ ID NO: 655	HepC1a segment 125	90 nts
SEQ ID NO: 656	Polypeptide encoded by SEQ ID NO: 655	30 aa
SEQ ID NO: 657	HepCla segment 126	90 nts
SEQ ID NO: 658	Polypeptide encoded by SEQ ID NO: 657	30 aa
SEQ ID NO: 659	HepC1a segment 127	90 nts
SEQ ID NO: 660	Polypeptide encoded by SEQ ID NO: 659	30 aa
SEQ ID NO: 661	HepCla segment 128	90 nts
SEQ ID NO: 662	Polypeptide encoded by SEQ ID NO: 661	30 aa
SEQ ID NO: 663	HepC1a segment 129	90 nts
SEQ ID NO: 664	Polypeptide encoded by SEQ ID NO: 663	30 aa
SEQ ID NO: 665	HepC1a segment 130	90 nts
SEQ ID NO: 666	Polypeptide encoded by SEQ ID NO: 665	30 aa
SEQ ID NO: 667	HepCla segment 131	90 nts
SEQ ID NO: 668	Polypeptide encoded by SEQ ID NO: 667	30 aa
SEQ ID NO: 669	HepCla segment 132	90 nts
SEQ ID NO: 670	Polypeptide encoded by SEQ ID NO: 669	30 aa

SEQUENCI ID NUMBER	r SLQUENCE  -	LENGTH
SEQ ID NO: 671	HepCla segment 133	90 nts
SEQ ID NO: 672	Polypeptide encoded by SEQ ID NO: 671	30 aa
SEQ ID NO: 673	HepCla segment 134	90 nts
SEQ ID NO: 674	Polypeptide encoded by SEQ ID NO: 673	30 aa
SEQ ID NO: 675	HepC1a segment 135	90 nts
SEQ ID NO: 676	Polypeptide encoded by SEQ ID NO: 675	30 aa
SEQ ID NO: 677	HepC1a segment 136	90 nts
SEQ ID NO: 678	Polypeptide encoded by SEQ ID NO: 677	30 aa
SEQ ID NO: 679	HepC1a segment 137	90 nts
SEQ ID NO: 680	Polypeptide encoded by SEQ ID NO: 679	30 aa
SEQ ID NO: 681	HepC1a segment 138	90 nts
SEQ ID NO: 682	Polypeptide encoded by SEQ ID NO: 681	30 aa
SEQ ID NO: 683	HepC1a segment 139	90 nts
SEQ ID NO: 684	Polypeptide encoded by SEQ ID NO: 683	30 aa
SEQ ID NO: 685	HepCla segment 140	90 nts
SEQ ID NO: 686	Polypeptide encoded by SEQ ID NO: 685	30 aa
SEQ ID NO: 687	HepCla segment 141	90 nts
SEQ ID NO: 688	Polypeptide encoded by SEQ ID NO: 687	30 aa
SEQ ID NO: 689	HepC1a segment 142	90 nts
SEQ ID NO: 690	Polypeptide encoded by SEQ ID NO: 689	30 aa
SEQ ID NO: 691	HepCla segment 143	90 nts
SEQ ID NO: 692	Polypeptide encoded by SEQ ID NO: 691	30 aa
SEQ ID NO: 693	HepCla segment 144	90 nts
SEQ ID NO: 694	Polypeptide encoded by SEQ ID NO: 693	30 aa

SEQUENCE D NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 695	HepCla segment 145	90 nts
SEQ ID NO: 696	Polypeptide encoded by SEQ ID NO: 695	30 aa
SEQ ID NO: 697	HepCla segment 146	90 nts
SEQ ID NO: 698	Polypeptide encoded by SEQ ID NO: 697	30 aa
SEQ ID NO: 699	HepCla segment 147	90 nts
SEQ ID NO: 700	Polypeptide encoded by SEQ ID NO: 699	30 aa
SEQ ID NO: 701	HepCla segment 148	90 nts
SEQ ID NO: 702	Polypeptide encoded by SEQ ID NO: 701	30 aa
SEQ ID NO: 703	HepC1a segment 149	90 nts
SEQ ID NO: 704	Polypeptide encoded by SEQ ID NO: 703	30 aa
SEQ ID NO: 705	HepC1a segment 150	90 nts
SEQ ID NO: 706	Polypeptide encoded by SEQ ID NO: 705	30 aa
SEQ ID NO: 707	HepC1a segment 151	90 nts
SEQ ID NO: 708	Polypeptide encoded by SEQ ID NO: 707	30 aa
SEQ ID NO: 709	HepCla segment 152	90 nts
SEQ ID NO: 710	Polypeptide encoded by SEQ ID NO: 709	30 aa
SEQ ID NO: 711	HepCla segment 153	90 nts
SEQ ID NO: 712	Polypeptide encoded by SEQ ID NO: 711	30 aa
SEQ ID NO: 713	HepCla segment 154	90 nts
SEQ ID NO: 714	Polypeptide encoded by SEQ ID NO: 713	30 aa
SEQ ID NO: 715	HepCla segment 155	90 nts
SEQ ID NO: 716	Polypeptide encoded by SEQ ID NO: 715	30 aa
SEQ ID NO: 717	HepCla segment 156	90 nts
SEQ ID NO: 718	Polypeptide encoded by SEQ ID NO: 717	30 aa

SEQUENCE ID NUMBER	STONEMCS	LENGTH
SEQ ID NO: 719	HepCla segment 157	90 nts
SEQ ID NO: 720	Polypeptide encoded by SEQ ID NO: 719	30 aa
SEQ ID NO: 721	HepCla segment 158	90 nts
SEQ ID NO: 722	Polypeptide encoded by SEQ ID NO: 721	30 aa
SEQ ID NO: 723	HepC1a segment 159	90 nts
SEQ ID NO: 724	Polypeptide encoded by SEQ ID NO: 723	30 aa
SEQ ID NO: 725	HepCla segment 160	90 nts
SEQ ID NO: 726	Polypeptide encoded by SEQ ID NO: 725	30 aa
SEQ ID NO: 727	HepCla segment 161	90 nts
SEQ ID NO: 728	Polypeptide encoded by SEQ ID NO: 727	30 aa
SEQ ID NO: 729	HepCla segment 162	90 nts
SEQ ID NO: 730	Polypeptide encoded by SEQ ID NO: 729	30 aa
SEQ ID NO: 731	HepCla segment 163	90 nts
SEQ ID NO: 732	Polypeptide encoded by SEQ ID NO: 731	30 aa
SEQ ID NO: 733	HepC1a segment 164	90 nts
SEQ ID NO: 734	Polypeptide encoded by SEQ ID NO: 733	30 aa
SEQ ID NO: 735	HepC1a segment 165	90 nts
SEQ ID NO: 736	Polypeptide encoded by SEQ ID NO: 735	30 aa
SEQ ID NO: 737	HepCla segment 166	90 nts
SEQ ID NO: 738	Polypeptide encoded by SEQ ID NO: 737	30 aa
SEQ ID NO: 739	HepCla segment 167	90 nts
SEQ ID NO: 740	Polypeptide encoded by SEQ ID NO: 739	30 aa
SEQ ID NO: 741	HepCla segment 168	90 nts
SEQ ID NO: 742	Polypeptide encoded by SEQ ID NO: 741	30 aa

SEQUENCE ID NUMBER	SEGUENCI	LENGTH
SEQ ID NO: 743	HepCla segment 169	90 nts
SEQ ID NO: 744	Polypeptide encoded by SEQ ID NO: 743	30 aa
SEQ ID NO: 745	HepCla segment 170	90 nts
SEQ ID NO: 746	Polypeptide encoded by SEQ ID NO: 745	30 aa
SEQ ID NO: 747	HepCla segment 171	90 nts
SEQ ID NO: 748	Polypeptide encoded by SEQ ID NO: 747	30 aa
SEQ ID NO: 749	HepCla segment 172	90 nts
SEQ ID NO: 750	Polypeptide encoded by SEQ ID NO: 749	30 aa
SEQ ID NO: 751	HepCla segment 173	90 nts
SEQ ID NO: 752	Polypeptide encoded by SEQ ID NO: 751	30 aa
SEQ ID NO: 753	HepCla segment 174	90 nts
SEQ ID NO: 754	Polypeptide encoded by SEQ ID NO: 753	30 aa
SEQ ID NO: 755	HepCla segment 175	90 nts
SEQ ID NO: 756	Polypeptide encoded by SEQ ID NO: 755	30 aa
<b>SEQ ID NO: 757</b>	HepCla segment 176	90 nts
SEQ ID NO: 758	Polypeptide encoded by SEQ ID NO: 757	30 aa
SEQ ID NO: 759	HepCla segment 177	90 nts
SEQ ID NO: 760	Polypeptide encoded by SEQ ID NO: 759	30 aa
SEQ ID NO: 761	HepCla segment 178	90 nts
SEQ ID NO: 762	Polypeptide encoded by SEQ ID NO: 761	30 aa
SEQ ID NO: 763	HepCla segment 179	90 nts
SEQ ID NO: 764	Polypeptide encoded by SEQ ID NO: 763	30 aa
SEQ ID NO: 765	HepC1a segment 180	90 nts
SEQ ID NO: 766	Polypeptide encoded by SEQ ID NO: 765	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 767	HepCla segment 181	90 nts
SEQ ID NO: 768	Polypeptide encoded by SEQ ID NO: 767	30 aa
SEQ ID NO: 769	HepC1a segment 182	90 nts
SEQ ID NO: 770	Polypeptide encoded by SEQ ID NO: 769	30 aa
SEQ ID NO: 771	HepC1a segment 183	90 nts
SEQ ID NO: 772	Polypeptide encoded by SEQ ID NO: 771	·30 aa
SEQ ID NO: 773	HepCla segment 184	90 nts
SEQ ID NO: 774	Polypeptide encoded by SEQ ID NO: 773	30 aa
SEQ ID NO: 775	HepC1a segment 185	90 nts
SEQ ID NO: 776	Polypeptide encoded by SEQ ID NO: 775	30 aa
SEQ ID NO: 777	HepCla segment 186	90 nts
SEQ ID NO: 778	Polypeptide encoded by SEQ ID NO: 777	30 aa
SEQ ID NO: 779	HepCla segment 187	90 nts
SEQ ID NO: 780	Polypeptide encoded by SEQ ID NO: 779	30 aa
SEQ ID NO: 781	HepCla segment 188	90 nts
SEQ ID NO: 782	Polypeptide encoded by SEQ ID NO: 781	30 aa
SEQ ID NO: 783	HepCla segment 189	90 nts
SEQ ID NO: 784	Polypeptide encoded by SEQ ID NO: 783	30 aa
SEQ ID NO: 785	HepCla segment 190	90 nts
SEQ ID NO: 786	Polypeptide encoded by SEQ ID NO: 785	30 aa
SEQ ID NO: 787	HepCla segment 191	90 nts
SEQ ID NO: 788	Polypeptide encoded by SEQ ID NO: 787	30 aa
SEQ ID NO: 789	HepC1a segment 192	90 nts
SEQ ID NO: 790	Polypeptide encoded by SEQ ID NO: 789	30 aa

SEQUENCE (D NUMBER	SEQUENCE .	LEMOTH
SEQ ID NO: 791	HepC1a segment 193	90 nts
SEQ ID NO: 792	Polypeptide encoded by SEQ ID NO: 791	30 aa
SEQ ID NO: 793	HepC1a segment 194	90 nts
SEQ ID NO: 794	Polypeptide encoded by SEQ ID NO: 793	30 aa
SEQ ID NO: 795	HepC1a segment 195	90 nts
SEQ ID NO: 796	Polypeptide encoded by SEQ ID NO: 795	30 aa
SEQ ID NO: 797	HepC1a segment 196	90 nts
SEQ ID NO: 798	Polypeptide encoded by SEQ ID NO: 797	30 aa
SEQ ID NO: 799	HepC1a segment 197	90 nts
SEQ ID NO: 800	Polypeptide encoded by SEQ ID NO: 799	30 aa
SEQ ID NO: 801	HepC1a segment 198	90 nts
SEQ ID NO: 802	Polypeptide encoded by SEQ ID NO: 801	30 aa
SEQ ID NO: 803	HepCla segment 199	90 nts
SEQ ID NO: 804	Polypeptide encoded by SEQ ID NO: 803	30 aa
SEQ ID NO: 805	HepC1a segment 200	90 nts
SEQ ID NO: 806	Polypeptide encoded by SEQ ID NO: 805	30 aa
SEQ ID NO: 807	HepC1a segment 201	45 nts
SEQ ID NO: 808	Polypeptide encoded by SEQ ID NO: 807	15 aa
SEQ ID NO: 809	HepC1a scrambled	17955 nts
SEQ ID NO: 810	Polypeptide encoded by SEQ ID NO: 809	5985 aa
SEQ ID NO: 811	HepC Cassette A	6065 nts
SEQ ID NO: 812	Polypeptide encoded by SEQ ID NO: 811	2011 aa
SEQ ID NO: 813	HepC Cassette B	6069 nts
SEQ ID NO: 814	Polypeptide encoded by SEQ ID NO: 813	2010 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 815	HepC Cassette C	6030 nts
SEQ ID NO: 816	Polypeptide encoded by SEQ ID NO: 815	1997 aa
SEQ ID NO: 817	gp100 consensus polypeptide	661 aa
SEQ ID NO: 818	MART consensus polypeptide	118 aa
SEQ ID NO: 819	TRP-1 consensus polypeptide	248 aa
SEQ ID NO: 820	Tyros consensus polypeptide	529 aa
SEQ ID NO: 821	TRP2 consensus polypeptide	519 aa
SEQ ID NO: 822	MC1R consensus polypeptide	317 aa
SEQ ID NO: 823	MUC1F consensus polypeptide	125 aa
SEQ ID NO: 824	MUC1R consensus polypeptide	312 aa
SEQ ID NO: 825	BAGE consensus polypeptide	43 aa
SEQ ID NO: 826	GAGE-1 consensus polypeptide	138 aa
SEQ ID NO: 827	gp100ln4 consensus polypeptide	51 aa
SEQ ID NO: 828	MAGE-1 consensus polypeptide	309 aa
SEQ ID NO: 829	MAGE-3 consensus polypeptide	314 aa
SEQ ID NO: 830	PRAME consensus polypeptide	509 aa
SEQ ID NO: 831	TRP2IN2 consensus polypeptide	54 aa
SEQ ID NO: 832	NYNSO1a consensus polypeptide	180 aa
SEQ ID NO: 833	NYNSO1b consensus polypeptide	58 aa
SEQ ID NO: 834	LAGE1 consensus polypeptide	180 aa
SEQ ID NO: 835	gp100 segment 1	90 nts
SEQ ID NO: 836	Polypeptide encoded by SEQ ID NO: 835	30 aa
SEQ ID NO: 837	gp100 segment 2	90 nts
SEQ ID NO: 838	Polypeptide encoded by SEQ ID NO: 837	30 aa

SEQUENCE D NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 839	gp100 segment 3	90 nts
SEQ ID NO: 840	Polypeptide encoded by SEQ ID NO: 839	30 aa
SEQ ID NO: 841	gp100 segment 4	90 nts
SEQ ID NO: 842	Polypeptide encoded by SEQ ID NO: 841	30 aa
SEQ ID NO: 843	gp100 segment 5	90 nts
SEQ ID NO: 844	Polypeptide encoded by SEQ ID NO: 843	30 aa
SEQ ID NO: 845	gp100 segment 6	90 nts
SEQ ID NO: 846	Polypeptide encoded by SEQ ID NO: 845	30 aa
SEQ ID NO: 847	gp100 segment 7	90 nts
SEQ ID NO: 848	Polypeptide encoded by SEQ ID NO: 847	30 aa
SEQ ID NO: 849	gp100 segment 8	90 nts
SEQ ID NO: 850	Polypeptide encoded by SEQ ID NO: 849	30 aa
SEQ ID NO: 851	gp100 segment 9	90 nts
SEQ ID NO: 852	Polypeptide encoded by SEQ ID NO: 851	30 aa
SEQ ID NO: 853	gp100 segment 10	90 nts
SEQ ID NO: 854	Polypeptide encoded by SEQ ID NO: 853	30 aa
SEQ ID NO: 855	gp100 segment 11	90 nts
SEQ ID NO: 856	Polypeptide encoded by SEQ ID NO: 855	30 aa
SEQ ID NO: 857	gp100 segment 12	90 nts
SEQ ID NO: 858	Polypeptide encoded by SEQ ID NO: 857	30 aa
SEQ ID NO: 859	gp100 segment 13	90 nts
SEQ ID NO: 860	Polypeptide encoded by SEQ ID NO: 859	30 aa
SEQ ID NO: 861	gp100 segment 14	90 nts
SEQ ID NO: 862	Polypeptide encoded by SEQ ID NO: 861	30 aa

SEQUENCI ID MUNBER	SIGUINCE	LENGTH
SEQ ID NO: 863	gp100 segment 15	90 nts
SEQ ID NO: 864	Polypeptide encoded by SEQ ID NO: 863	30 aa
SEQ ID NO: 865	gp100 segment 16	90 nts
SEQ ID NO: 866	Polypeptide encoded by SEQ ID NO: 865	30 aa
SEQ ID NO: 867	gp100 segment 17	90 nts
SEQ ID NO: 868	Polypeptide encoded by SEQ ID NO: 867	30 aa
SEQ ID NO: 869	gp100 segment 18	90 nts
SEQ ID NO: 870	Polypeptide encoded by SEQ ID NO: 869	30 aa
SEQ ID NO: 871	gp100 segment 19	90 nts
SEQ ID NO: 872	Polypeptide encoded by SEQ ID NO: 871	30 aa
SEQ ID NO: 873	gp100 segment 20	90 nts
SEQ ID NO: 874	Polypeptide encoded by SEQ ID NO: 873	30 aa
SEQ ID NO: 875	gp100 segment 21	90 nts
SEQ ID NO: 876	Polypeptide encoded by SEQ ID NO: 875	30 aa
SEQ ID NO: 877	gp100 segment 22	90 nts
SEQ ID NO: 878	Polypeptide encoded by SEQ ID NO: 877	30 aa
SEQ ID NO: 879	gp100 segment 23	90 nts
SEQ ID NO: 880	Polypeptide encoded by SEQ ID NO: 879	30 aa
SEQ ID NO: 881	gp100 segment 24	90 nts
SEQ ID NO: 882	Polypeptide encoded by SEQ ID NO: 881	30 aa
SEQ ID NO: 883	gp100 segment 25	90 nts
SEQ ID NO: 884	Polypeptide encoded by SEQ ID NO: 883	30 aa
<b>SEQ ID NO: 885</b>	gp100 segment 26	90 nts
SEQ ID NO: 886	Polypeptide encoded by SEQ ID NO: 885	30 aa

NGUENCI D NUMBIR	SEQUENCE 	LENGTH
SEQ ID NO: 887	gp100 segment 27	90 nts
SEQ ID NO: 888	Polypeptide encoded by SEQ ID NO: 887	30 aa
SEQ ID NO: 889	gp100 segment 28	90 nts
SEQ ID NO: 890	Polypeptide encoded by SEQ ID NO: 889	30 aa
SEQ ID NO: 891	gp100 segment 29	90 nts
SEQ ID NO: 892	Polypeptide encoded by SEQ ID NO: 891	30 aa
SEQ ID NO: 893	gp100 segment 30	90 nts
SEQ ID NO: 894	Polypeptide encoded by SEQ ID NO: 893	30 aa
SEQ ID NO: 895	gp100 segment 31	90 nts
SEQ ID NO: 896	Polypeptide encoded by SEQ ID NO: 895	30 aa
SEQ ID NO: 897	gp100 segment 32	90 nts
SEQ ID NO: 898	Polypeptide encoded by SEQ ID NO: 897	30 aa
SEQ ID NO: 899	gp100 segment 33	90 nts
SEQ ID NO: 900	Polypeptide encoded by SEQ ID NO: 899	30 aa
SEQ ID NO: 901	gp100 segment 34	90 nts
SEQ ID NO: 902	Polypeptide encoded by SEQ ID NO: 901	30 aa
SEQ ID NO: 903	gp100 segment 35	90 nts
SEQ ID NO: 904	Polypeptide encoded by SEQ ID NO: 903	30 aa
SEQ ID NO: 905	gp100 segment 36	90 nts
SEQ ID NO: 906	Polypeptide encoded by SEQ ID NO: 905	30 aa
SEQ ID NO: 907	gp100 segment 37	90 nts
SEQ ID NO: 908	Polypeptide encoded by SEQ ID NO: 907	30 aa
SEQ ID NO: 909	gp100 segment 38	90 nts
SEQ ID NO: 910	Polypeptide encoded by SEQ ID NO: 909	30 aa

MOLENCI ID MUMBER	: Segvenci	LINGTH
SEQ ID NO: 911	gp100 segment 39	90 nts
SEQ ID NO: 912	Polypeptide encoded by SEQ ID NO: 911	30 aa
SEQ ID NO: 913	gp100 segment 40	90 nts
SEQ ID NO: 914	Polypeptide encoded by SEQ ID NO: 913	30 aa
SEQ ID NO: 915	gp100 segment 41	90 nts
SEQ ID NO: 916	Polypeptide encoded by SEQ ID NO: 915	30 aa
SEQ ID NO: 917	gp100 segment 42	90 nts
SEQ ID NO: 918	Polypeptide encoded by SEQ ID NO: 917	30 aa
SEQ ID NO: 919	gp100 segment 43	90 nts
SEQ ID NO: 920	Polypeptide encoded by SEQ ID NO: 919	30 aa
SEQ ID NO: 921	gp100 segment 44	60nts
SEQ ID NO: 922	Polypeptide encoded by SEQ ID NO: 921	20 aa
SEQ ID NO: 923	MART segment 1	90 nts
SEQ ID NO: 924	Polypeptide encoded by SEQ ID NO: 923	30 aa
SEQ ID NO: 925	MART segment 2	90 nts
SEQ ID NO: 926	Polypeptide encoded by SEQ ID NO: 925	30 aa
SEQ ID NO: 927	MART segment 3	90 nts
SEQ ID NO: 928	Polypeptide encoded by SEQ ID NO: 927	30 aa
SEQ ID NO: 929	MART segment 4	90 nts
SEQ ID NO: 930	Polypeptide encoded by SEQ ID NO: 929	30 aa
SEQ ID NO: 931	MART segment 5	90 nts
SEQ ID NO: 932	Polypeptide encoded by SEQ ID NO: 931	30 aa
SEQ ID NO: 933	MART segment 6	90 nts
SEQ ID NO: 934	Polypeptide encoded by SEQ ID NO: 933	30 aa

SEQUENCI D MUNSIR	NEGOTO CE	LENGTH
SEQ ID NO: 935	MART segment 7	90 nts
SEQ ID NO: 936	Polypeptide encoded by SEQ ID NO: 935	30 aa
SEQ ID NO: 937	MART segment 8	51 nts
SEQ ID NO: 938	Polypeptide encoded by SEQ ID NO: 937	17 aa
SEQ ID NO: 939	trp-1 segment 1	90 nts
SEQ ID NO: 940	Polypeptide encoded by SEQ ID NO: 939	30 aa
SEQ ID NO: 941	trp-1 segment 2	90 nts
SEQ ID NO: 942	Polypeptide encoded by SEQ ID NO: 941	30 aa
SEQ ID NO: 943	trp-1 segment 3	90 nts
SEQ ID NO: 944	Polypeptide encoded by SEQ ID NO: 943	30 aa
SEQ ID NO: 945	trp-1 segment 4	90 nts
SEQ ID NO: 946	Polypeptide encoded by SEQ ID NO: 945	30 aa
SEQ ID NO: 947	trp-1 segment 5	90 nts
SEQ ID NO: 948	Polypeptide encoded by SEQ ID NO: 947	30 aa
SEQ ID NO: 949	trp-1 segment 6	90 nts
SEQ ID NO: 950	Polypeptide encoded by SEQ ID NO: 949	30 aa
SEQ ID NO: 951	trp-1 segment 7	90 nts
SEQ ID NO: 952	Polypeptide encoded by SEQ ID NO: 951	30 aa
SEQ ID NO: 953	trp-1 segment 8	90 nts
SEQ ID NO: 954	Polypeptide encoded by SEQ ID NO: 953	30 aa
SEQ ID NO: 955	trp-1 segment 9	90 nts
SEQ ID NO: 956	Polypeptide encoded by SEQ ID NO: 955	30 aa
SEQ ID NO: 957	trp-1 segment 10	90 nts
SEQ ID NO: 958	Polypeptide encoded by SEQ ID NO: 957	30 aa

MIQUENCE D MINIBER	MOJENCI	LENGTH
SEQ ID NO: 959	trp-1 segment 11	90 nts
SEQ ID NO: 960	Polypeptide encoded by SEQ ID NO: 959	30 aa
SEQ ID NO: 961	trp-1 segment 12	90 nts
SEQ ID NO: 962	Polypeptide encoded by SEQ ID NO: 961	30 aa
SEQ ID NO: 963	trp-1 segment 13	90 nts
SEQ ID NO: 964	Polypeptide encoded by SEQ ID NO: 963	30 aa
SEQ ID NO: 965	trp-1 segment 14	90 nts
SEQ ID NO: 966	Polypeptide encoded by SEQ ID NO: 965	30 aa
SEQ ID NO: 967	trp-1 segment 15	90 nts
SEQ ID NO: 968	Polypeptide encoded by SEQ ID NO: 967	30 aa
SEQ ID NO: 969	trp-1 segment 16	81 nts
SEQ ID NO: 970	Polypeptide encoded by SEQ ID NO: 969	27 aa
SEQ ID NO: 971	tyros segment 1	90 nts
SEQ ID NO: 972	Polypeptide encoded by SEQ ID NO: 971	30 aa
SEQ ID NO: 973	tyros segment 2	90 nts
SEQ ID NO: 974	Polypeptide encoded by SEQ ID NO: 973	30 aa
SEQ ID NO: 975	tyros segment 3	90 nts
SEQ ID NO: 976	Polypeptide encoded by SEQ ID NO: 975	30 aa
SEQ ID NO: 977	tyros segment 4	90 nts
SEQ ID NO: 978	Polypeptide encoded by SEQ ID NO: 977	30 aa
SEQ ID NO: 979	tyros segment 5	90 nts
SEQ ID NO: 980	Polypeptide encoded by SEQ ID NO: 979	30 aa
SEQ ID NO: 981	tyros segment 6	90 nts
SEQ ID NO: 982	Polypeptide encoded by SEQ ID NO: 981	30 aa

SEQUENCE ID HUMBER	SEQUENCE	LENGTH
SEQ ID NO: 983	tyros segment 7	90 nts
SEQ ID NO: 984	Polypeptide encoded by SEQ ID NO: 983	30 aa
SEQ ID NO: 985	tyros segment 8	90 nts
SEQ ID NO: 986	Polypeptide encoded by SEQ ID NO: 985	30 aa
SEQ ID NO: 987	tyros segment 9	90 nts
SEQ ID NO: 988	Polypeptide encoded by SEQ ID NO: 987	30 aa
SEQ ID NO: 989	tyros segment 10	90 nts
SEQ ID NO: 990 .	Polypeptide encoded by SEQ ID NO: 989	30 aa
SEQ ID NO: 991	tyros segment 11	90 nts
SEQ ID NO: 992	Polypeptide encoded by SEQ ID NO: 991	30 aa
SEQ ID NO: 993	tyros segment 12	90 nts
SEQ ID NO: 994	Polypeptide encoded by SEQ ID NO: 993	30 aa
SEQ ID NO: 995	tyros segment 13	90 nts
SEQ ID NO: 996	Polypeptide encoded by SEQ ID NO: 995	30 aa
SEQ ID NO: 997	tyros segment 14	90 nts
SEQ ID NO: 998	Polypeptide encoded by SEQ ID NO: 997	30 aa
SEQ ID NO: 999	tyros segment 15	90 nts
SEQ ID NO: 1000	Polypeptide encoded by SEQ ID NO: 999	30 aa
SEQ ID NO: 1001	tyros segment 16	90 nts
SEQ ID NO: 1002	Polypeptide encoded by SEQ ID NO: 1001	30 aa
SEQ ID NO: 1003	tyros segment 17	90 nts
SEQ ID NO: 1004	Polypeptide encoded by SEQ ID NO: 1003	30 aa
SEQ ID NO: 1005	tyros segment 18	90 nts
SEQ ID NO: 1006	Polypeptide encoded by SEQ ID NO: 1005	30 aa

SEQUENCE ID NUMBER	i Sequence	Length
SEQ ID NO: 1007	tyros segment 19	90 nts
SEQ ID NO: 1008	Polypeptide encoded by SEQ ID NO: 1007	30 aa
SEQ ID NO: 1009	tyros segment 20	90 nts
SEQ ID NO: 1010	Polypeptide encoded by SEQ ID NO: 1009	30 aa
SEQ ID NO: 1011	tyros segment 21	90 nts
SEQ ID NO: 1012	Polypeptide encoded by SEQ ID NO: 1011	30 aa
SEQ ID NO: 1013	tyros segment 22	90 nts
SEQ ID NO: 1014	Polypeptide encoded by SEQ ID NO: 1013	30 aa
SEQ ID NO: 1015	tyros segment 23	90 nts
SEQ ID NO: 1016	Polypeptide encoded by SEQ ID NO: 1015	30 aa
SEQ ID NO: 1017	tyros segment 24	90 nts
SEQ ID NO: 1018	Polypeptide encoded by SEQ ID NO: 1017	30 aa
SEQ ID NO: 1019	tyros segment 25	90 nts
<b>SEQ ID NO: 1020</b>	Polypeptide encoded by SEQ ID NO: 1019	30 aa
SEQ ID NO: 1021	tyros segment 26	90 nts
SEQ ID NO: 1022	Polypeptide encoded by SEQ ID NO: 1021	30 aa
SEQ ID NO: 1023	tyros segment 27	90 nts
SEQ ID NO: 1024	Polypeptide encoded by SEQ ID NO: 1023	30 aa
SEQ ID NO: 1025	tyros segment 28	90 nts
SEQ ID NO: 1026	Polypeptide encoded by SEQ ID NO: 1025	30 aa
SEQ ID NO: 1027	tyros segment 29	90 nts
SEQ ID NO: 1028	Polypeptide encoded by SEQ ID NO: 1027	30 aa
SEQ ID NO: 1029	tyros segment 30	90 nts
SEQ ID NO: 1030	Polypeptide encoded by SEQ ID NO: 1029	30 aa

NOUINCE (D) NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 1031	tyros segment 31	90 nts
SEQ ID NO: 1032	Polypeptide encoded by SEQ ID NO: 1031	30 aa
SEQ ID NO: 1033	tyros segment 32	90 nts
SEQ ID NO: 1034	Polypeptide encoded by SEQ ID NO: 1033	30 aa
SEQ ID NO: 1035	tyros segment 33	90 nts
SEQ ID NO: 1036	Polypeptide encoded by SEQ ID NO: 1035	30 aa
SEQ ID NO: 1037	tyros segment 34	90 nts
SEQ ID NO: 1038	Polypeptide encoded by SEQ ID NO: 1037	30 aa
SEQ ID NO: 1039	tyros segment 35	69 nts
SEQ ID NO: 1040	Polypeptide encoded by SEQ ID NO: 1039	23 aa
SEQ ID NO: 1041	trp2 segment 1	90 nts
SEQ ID NO: 1042	Polypeptide encoded by SEQ ID NO: 1041	30 aa
SEQ ID NO: 1043.	trp2 segment 2	90 nts
SEQ ID NO: 1044	Polypeptide encoded by SEQ ID NO: 1043	30 aa
SEQ ID NO: 1045	trp2 segment 3	90 nts
SEQ ID NO: 1046	Polypeptide encoded by SEQ ID NO: 1045	30 aa
SEQ ID NO: 1047	trp2 segment 4	90 nts
SEQ ID NO: 1048	Polypeptide encoded by SEQ ID NO: 1047	30 aa
SEQ ID NO: 1049	trp2 segment 5	90 nts
SEQ ID NO: 1050	Polypeptide encoded by SEQ ID NO: 1049	30 aa
SEQ ID NO: 1051	trp2 segment 6	.90 nts
SEQ ID NO: 1052	Polypeptide encoded by SEQ ID NO: 1051	30 aa
SEQ ID NO: 1053	trp2 segment 7	90 nts
·SEQ ID NO: 1054	Polypeptide encoded by SEQ ID NO: 1053	30 aa

SEQUENCE ED NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1055	trp2 segment 8	90 nts
SEQ ID NO: 1056	Polypeptide encoded by SEQ ID NO: 1055	30 aa
SEQ ID NO: 1057	trp2 segment 9	90 nts
SEQ ID NO: 1058	Polypeptide encoded by SEQ ID NO: 1057	30 aa
SEQ ID NO: 1059	trp2 segment 10	90 nts
SEQ ID NO: 1060	Polypeptide encoded by SEQ ID NO: 1059	30 aa
SEQ ID NO: 1061	trp2 segment 11	90 nts
SEQ ID NO: 1062	Polypeptide encoded by SEQ ID NO: 1061	30 aa
SEQ ID NO: 1063	trp2 segment 12	90 nts
SEQ ID NO: 1064	Polypeptide encoded by SEQ ID NO: 1063	30 aa
SEQ ID NO: 1065	trp2 segment 13	90 nts
SEQ ID NO: 1066	Polypeptide encoded by SEQ ID NO: 1065	30 aa
SEQ ID NO: 1067	trp2 segment 14	90 nts
SEQ ID NO: 1068	Polypeptide encoded by SEQ ID NO: 1067	30 aa
SEQ ID NO: 1069	trp2 segment 15	90 nts
SEQ ID NO: 1070	Polypeptide encoded by SEQ ID NO: 1069	30 aa
SEQ ID NO: 1071	trp2 segment 16	90 nts
SEQ ID NO: 1072	Polypeptide encoded by SEQ ID NO: 1071	30 aa
SEQ ID NO: 1073	trp2 segment 17	90 nts
SEQ ID NO: 1074	Polypeptide encoded by SEQ ID NO: 1073	30 aa
SEQ ID NO: 1075	trp2 segment 18	90 nts
SEQ ID NO: 1076	Polypeptide encoded by SEQ ID NO: 1075	30 aa
SEQ ID NO: 1077	trp2 segment 19	90 nts
SEQ ID NO: 1078	Polypeptide encoded by SEQ ID NO: 1077	30 aa

SEQUENCE ID NAMBER	SIQUIMOI	LINGTH
SEQ ID NO: 1079	trp2 segment 20	90 nts
SEQ ID NO: 1080	Polypeptide encoded by SEQ ID NO: 1079	30 aa 、
SEQ ID NO: 1081	trp2 segment 21	90 nts
SEQ ID NO: 1082	Polypeptide encoded by SEQ ID NO: 1081	30 aa
SEQ ID NO: 1083	trp2 segment 22	90 nts
SEQ ID NO: 1084	Polypeptide encoded by SEQ ID NO: 1083	30 aa
SEQ ID NO: 1085	trp2 segment 23	90 nts
SEQ ID NO: 1086	Polypeptide encoded by SEQ ID NO: 1085	30 aa
SEQ ID NO: 1087	trp2 segment 24	90 nts
SEQ ID NO: 1088	Polypeptide encoded by SEQ ID NO: 1087	30 aa
SEQ ID NO: 1089	trp2 segment 25	90 nts
SEQ ID NO: 1090	Polypeptide encoded by SEQ ID NO: 1089	30 aa .
SEQ ID NO: 1091	trp2 segment 26	90 nts
SEQ ID NO: 1092	Polypeptide encoded by SEQ ID NO: 1091	30 aa
SEQ ID NO: 1093	trp2 segment 27	90 nts
SEQ ID NO: 1094	Polypeptide encoded by SEQ ID NO: 1093	30 aa
SEQ ID NO: 1095	trp2 segment 28	90 nts
SEQ ID NO: 1096	Polypeptide encoded by SEQ ID NO: 1095	30 aa
SEQ ID NO: 1097	trp2 segment 29	90 nts
SEQ ID NO: 1098	Polypeptide encoded by SEQ ID NO: 1097	30 aa
SEQ ID NO: 1099	trp2 segment 30	90 nts
SEQ ID NO: 1100	Polypeptide encoded by SEQ ID NO: 1099	30 aa
SEQ ID NO: 1101	trp2 segment 31	90 nts
SEQ ID NO: 1102	Polypeptide encoded by SEQ ID NO: 1101	30 aa

MOVENOLD	i MOUTINGI	LENGTH
NUMBER		
SEQ ID NO: 1103	trp2 segment 32	90 nts
SEQ ID NO: 1104	Polypeptide encoded by SEQ ID NO: 1103	30 aa
SEQ ID NO: 1105	trp2 segment 33	90 nts
SEQ ID NO: 1106	Polypeptide encoded by SEQ ID NO: 1105	30 aa
SEQ ID NO: 1107	trp2 segment 34	84 nts
SEQ ID NO: 1108	Polypeptide encoded by SEQ ID NO: 1107	28 aa
SEQ ID NO: 1109	MC1R segment 1	90 nts
SEQ ID NO: 1110	Polypeptide encoded by SEQ ID NO: 1109	30 aa
SEQ ID NO: 1111	MC1R segment 2	90 nts
SEQ ID NO: 1112	Polypeptide encoded by SEQ ID NO: 1111	30 aa
SEQ ID NO: 1113	MC1R segment 3	90 nts
SEQ ID NO: 1114	Polypeptide encoded by SEQ ID NO: 1113	30 aa
SEQ ID NO: 1115	MC1R segment 4	90 nts
SEQ ID NO: 1116	Polypeptide encoded by SEQ ID NO: 1115	30 aa
SEQ ID NO: 1117	MC1R segment 5	90 nts
SEQ ID NO: 1118	Polypeptide encoded by SEQ ID NO: 1117	30 aa
SEQ ID NO: 1119	MC1R segment 6	90 nts
SEQ ID NO: 1120	Polypeptide encoded by SEQ ID NO: 1119	30 aa
SEQ ID NO: 1121	MC1R segment 7	90 nts
SEQ ID NO: 1122	Polypeptide encoded by SEQ ID NO: 1121	30 aa
SEQ ID NO: 1123	MC1R segment 8	90 nts
SEQ ID NO: 1124	Polypeptide encoded by SEQ ID NO: 1123	30 aa
SEQ ID NO: 1125	MC1R segment 9	90 nts
SEQ ID NO: 1126	Polypeptide encoded by SEQ ID NO: 1125	30 aa

SIQUENCE ID NUMBER	SEQUENCE	<u>uength</u>
SEQ ID NO: 1127	MC1R segment 10	90 nts
SEQ ID NO: 1128	Polypeptide encoded by SEQ ID NO: 1127	30 aa
SEQ ID NO: 1129	MC1R segment 11	90 nts
SEQ ID NO: 1130	Polypeptide encoded by SEQ ID NO: 1129	30 aa
SEQ ID NO: 1131	MC1R segment 12	90 nts
SEQ ID NO: 1132	Polypeptide encoded by SEQ ID NO: 1131	30 aa
SEQ ID NO: 1133	MC1R segment 13	90 nts
SEQ ID NO: 1134	Polypeptide encoded by SEQ ID NO: 1133	30 aa
SEQ ID NO: 1135	MC1R segment 14	90 nts
SEQ ID NO: 1136	Polypeptide encoded by SEQ ID NO: 1135	30 aa
SEQ ID NO: 1137	MC1R segment 15	90 nts
SEQ ID NO: 1138	Polypeptide encoded by SEQ ID NO: 1137	30 aa
SEQ ID NO: 1139	MC1R segment 16	90 nts
SEQ ID NO: 1140	Polypeptide encoded by SEQ ID NO: 1139	30 aa
SEQ ID NO: 1141	MC1R segment 17	90 nts
SEQ ID NO: 1142	Polypeptide encoded by SEQ ID NO: 1141	30 aa
SEQ ID NO: 1143	MC1R segment 18	90 nts
SEQ ID NO: 1144	Polypeptide encoded by SEQ ID NO: 1143	30 aa
SEQ ID NO: 1145	MC1R segment 19	90 nts
SEQ ID NO: 1146	Polypeptide encoded by SEQ ID NO: 1145	30 aa
SEQ ID NO: 1147	MC1R segment 20	90 nts
SEQ ID NO: 1148	Polypeptide encoded by SEQ ID NO: 1147	30 aa
SEQ ID NO: 1149	MC1R segment 21	63 nts
SEQ ID NO: 1150	Polypeptide encoded by SEQ ID NO: 1149	21 aa

SEQUENCE DO	SECUTENCE	1ENGTH
MUNBLR		
SEQ ID NO: 1151	MUC1F segment 1	90 nts
SEQ ID NO: 1152	Polypeptide encoded by SEQ ID NO: 1151	30 aa
SEQ ID NO: 1153	MUC1F segment 2	90 nts
SEQ ID NO: 1154	Polypeptide encoded by SEQ ID NO: 1153	30 aa
SEQ ID NO: 1155	MUC1F segment 3	90 nts
SEQ ID NO: 1156	Polypeptide encoded by SEQ ID NO: 1155	30 aa
SEQ ID NO: 1157	MUC1F segment 4	90 nts
SEQ ID NO: 1158	Polypeptide encoded by SEQ ID NO: 1157	30 aa
SEQ ID NO: 1159	MUC1F segment 5	90 nts
SEQ ID NO: 1160	Polypeptide encoded by SEQ ID NO: 1159	30 aa
SEQ ID NO: 1161	MUC1F segment 6	90 nts
SEQ ID NO: 1162	Polypeptide encoded by SEQ ID NO: 1161	30 aa
SEQ ID NO: 1163	MUC1F segment 7	90 nts
SEQ ID NO: 1164	Polypeptide encoded by SEQ ID NO: 1163	30 aa
SEQ ID NO: 1165	MUC1F segment 8	72 nts
SEQ ID NO: 1166	Polypeptide encoded by SEQ ID NO: 1165	24 aa
SEQ ID NO: 1167	MUC1R segment 1	90 nts
SEQ ID NO: 1168	Polypeptide encoded by SEQ ID NO: 1167	30 aa
SEQ ID NO: 1169	MUC1R segment 2	90 nts
SEQ ID NO: 1170	Polypeptide encoded by SEQ ID NO: 1169	30 aa
SEQ ID NO: 1171	MUC1R segment 3	90 nts
SEQ ID NO: 1172	Polypeptide encoded by SEQ ID NO: 1171	30 aa
SEQ ID NO: 1173	MUC1R segment 4	90 nts
SEQ ID NO: 1174	Polypeptide encoded by SEQ ID NO: 1173	30 aa

SIQUENCI ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1175	MUC1R segment 5	90 nts
SEQ ID NO: 1176	Polypeptide encoded by SEQ ID NO: 1175	30 aa
SEQ ID NO: 1177	MUC1R segment 6	90 nts
SEQ ID NO: 1178	Polypeptide encoded by SEQ ID NO: 1177	30 aa
SEQ ID NO: 1179	MUC1R segment 7	90 nts
SEQ ID NO: 1180	Polypeptide encoded by SEQ ID NO: 1179	30 aa
SEQ ID NO: 1181	MUC1R segment 8	90 nts
SEQ ID NO: 1182	Polypeptide encoded by SEQ ID NO: 1181	30 aa
SEQ ID NO: 1183	MUC1R segment 9	90 nts
SEQ ID NO: 1184	Polypeptide encoded by SEQ ID NO: 1183	30 aa
SEQ ID NO: 1185	MUC1R segment 10	90 nts .
SEQ ID NO: 1186	Polypeptide encoded by SEQ ID NO: 1185	30 aa
SEQ ID NO: 1187	MUC1R segment 11	90 nts
SEQ ID NO: 1188	Polypeptide encoded by SEQ ID NO: 1187	30 aa
SEQ ID NO: 1189	MUC1R segment 12	90 nts
SEQ ID NO: 1190	Polypeptide encoded by SEQ ID NO: 1189	30 aa
SEQ ID NO: 1191	MUC1R segment 13	90 nts
SEQ ID NO: 1192	Polypeptide encoded by SEQ ID NO: 1191	30 aa
SEQ ID NO: 1193	MUC1R segment 14	90 nts
SEQ ID NO: 1194	Polypeptide encoded by SEQ ID NO: 1193	30 aa
SEQ ID NO: 1195	MUC1R segment 15	90 nts
SEQ ID NO: 1196	Polypeptide encoded by SEQ ID NO: 1195	30 aa
SEQ ID NO: 1197	MUC1R segment 16	90 nts
SEQ ID NO: 1198	Polypeptide encoded by SEQ ID NO: 1197	30 aa

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MQUENCI D NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1199	MUC1R segment 17	90 nts
SEQ ID NO: 1200	Polypeptide encoded by SEQ ID NO: 1199	30 aa
SEQ ID NO: 1201	MUC1R segment 18	90 nts
SEQ ID NO: 1202	Polypeptide encoded by SEQ ID NO: 1201	30 aa
SEQ ID NO: 1203	MUC1R segment 19	90 nts
SEQ ID NO: 1204	Polypeptide encoded by SEQ ID NO: 1203	30 aa
SEQ ID NO: 1205	MUC1R segment 20	90 nts
SEQ ID NO: 1206	Polypeptide encoded by SEQ ID NO: 1205	30 aa
SEQ ID NO: 1207	MUC1R segment 21	48 nts
SEQ ID NO: 1208	Polypeptide encoded by SEQ ID NO: 1207	16 aa
SEQ ID NO: 1209	Differentiation Savine	16638 nts
SEQ ID NO: 1210	Polypeptide encoded by SEQ ID NO: 1209	5546 aa
SEQ ID NO: 1211	BAGE segment 1	90 nts
SEQ ID NO: 1212	Polypeptide encoded by SEQ ID NO: 1211	30 aa
SEQ ID NO: 1213	BAGE segment 2	90 nts
SEQ ID NO: 1214	Polypeptide encoded by SEQ ID NO: 1213	30 aa
SEQ ID NO: 1215	BAGE segment 3	51 nts
SEQ ID NO: 1216	Polypeptide encoded by SEQ ID NO: 1215	17 aa
SEQ ID NO: 1217	GAGE-1 segment 1	90 nts
SEQ ID NO: 1218	Polypeptide encoded by SEQ ID NO: 1217	30 aa
SEQ ID NO: 1219	GAGE-1 segment 2	90 nts
SEQ ID NO: 1220	Polypeptide encoded by SEQ ID NO: 1219	30 aa
SEQ ID NO: 1221	GAGE-1 segment 3	90 nts
SEQ ID NO: 1222	Polypeptide encoded by SEQ ID NO: 1221	30 aa

SIÇUINCI D NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1223	GAGE-1 segment 4	90 nts
SEQ ID NO: 1224	Polypeptide encoded by SEQ ID NO: 1223	30 aa
SEQ ID NO: 1225	GAGE-1 segment 5	90 nts
SEQ ID NO: 1226	Polypeptide encoded by SEQ ID NO: 1225	30 aa
SEQ ID NO: 1227	GAGE-1 segment 6	90 nts
SEQ ID NO: 1228	Polypeptide encoded by SEQ ID NO: 1227	30 aa
SEQ ID NO: 1229	GAGE-1 segment 7	90 nts
SEQ ID NO: 1230	Polypeptide encoded by SEQ ID NO: 1229	30 aa
SEQ ID NO: 1231	GAGE-1 segment 8	90 nts
SEQ ID NO: 1232	Polypeptide encoded by SEQ ID NO: 1231	30 aa
SEQ ID NO: 1233	GAGE-1 segment 9	66 nts
SEQ ID NO: 1234	Polypeptide encoded by SEQ ID NO: 1233	22 aa
SEQ ID NO: 1235	gp100ln4 segment 1	90 nts
SEQ ID NO: 1236	Polypeptide encoded by SEQ ID NO: 1235	30 aa
SEQ ID NO: 1237	gp100ln4 segment 2	90 nts
SEQ ID NO: 1238	Polypeptide encoded by SEQ ID NO: 1237	30 aa
SEQ ID NO: 1239	gp100ln4 segment 3	75 nts
SEQ ID NO: 1240	Polypeptide encoded by SEQ ID NO: 1239	25 aa
SEQ ID NO: 1241	MAGE-1 segment 1	90 nts
SEQ ID NO: 1242	Polypeptide encoded by SEQ ID NO: 1241	30 aa
SEQ ID NO: 1243	MAGE-1 segment 2	90 nts
SEQ ID NO: 1244	Polypeptide encoded by SEQ ID NO: 1243	30 aa
SEQ ID NO: 1245	MAGE-1 segment 3	90 nts
SEQ ID NO: 1246	Polypeptide encoded by SEQ ID NO: 1245	30 aa

SEQUENCE ID MUNIBER	SIQUENCE	LINGTH
SEQ ID NO: 1247	MAGE-1 segment 4	90 nts
SEQ ID NO: 1248	Polypeptide encoded by SEQ ID NO: 1247	30 aa
SEQ ID NO: 1249	MAGE-1 segment 5	90 nts
SEQ ID NO: 1250	Polypeptide encoded by SEQ ID NO: 1249	30 aa
SEQ ID NO: 1251	MAGE-1 segment 6	90 nts
SEQ ID NO: 1252	Polypeptide encoded by SEQ ID NO: 1251	30 aa
SEQ ID NO: 1253	MAGE-1 segment 7	90 nts
SEQ ID NO: 1254	Polypeptide encoded by SEQ ID NO: 1253	30 aa
SEQ ID NO: 1255	MAGE-1 segment 8	90 nts
SEQ ID NO: 1256	Polypeptide encoded by SEQ ID NO: 1255	30 aa
SEQ ID NO: 1257	MAGE-1 segment 9	90 nts
SEQ ID NO: 1258	Polypeptide encoded by SEQ ID NO: 1257	30 aa
SEQ ID NO: 1259	MAGE-1 segment 10	90 nts
SEQ ID NO: 1260	Polypeptide encoded by SEQ ID NO: 1259	30 aa
SEQ ID NO: 1261	MAGE-1 segment 11	90 nts
SEQ ID NO: 1262	Polypeptide encoded by SEQ ID NO: 1261	30 aa
SEQ ID NO: 1263	MAGE-1 segment 12	90 nts
SEQ ID NO: 1264	Polypeptide encoded by SEQ ID NO: 1263	30 aa
SEQ ID NO: 1265	MAGE-1 segment 13	90 nts
SEQ ID NO: 1266	Polypeptide encoded by SEQ ID NO: 1265	30 aa
SEQ ID NO: 1267	MAGE-1 segment 14.	90 nts
SEQ ID NO: 1268	Polypeptide encoded by SEQ ID NO: 1267	30 aa
SEQ ID NO: 1269	MAGE-1 segment 15	90 nts
SEQ ID NO: 1270	Polypeptide encoded by SEQ ID NO: 1269	30 aa

SEQUENCE ID	SIQUENCE	LENGTH
NUMBER	244074	:
SEQ ID NO: 1271	MAGE-1 segment 16	90 nts
SEQ ID NO: 1272	Polypeptide encoded by SEQ ID NO: 1271	30 aa
SEQ ID NO: 1273	MAGE-1 segment 17	90 nts
SEQ ID NO: 1274	Polypeptide encoded by SEQ ID NO: 1273	30 aa
SEQ ID NO: 1275	MAGE-1 segment 18	90 nts
SEQ ID NO: 1276	Polypeptide encoded by SEQ ID NO: 1275	30 aa
SEQ ID NO: 1277	MAGE-1 segment 19	90 nts
SEQ ID NO: 1278	Polypeptide encoded by SEQ ID NO: 1277	30 aa
SEQ ID NO: 1279	MAGE-1 segment 20	84 nts
SEQ ID NO: 1280	Polypeptide encoded by SEQ ID NO: 1279	28 aa
SEQ ID NO: 1281	MAGE-3 segment 1	90 nts
SEQ ID NO: 1282	Polypeptide encoded by SEQ ID NO: 1281	30 aa
SEQ ID NO: 1283	MAGE-3 segment 2	90 nts
SEQ ID NO: 1284	Polypeptide encoded by SEQ ID NO: 1283	30 aa
SEQ ID NO: 1285	MAGE-3 segment 3	90 nts
SEQ ID NO: 1286	Polypeptide encoded by SEQ ID NO: 1285	30 aa
SEQ ID NO: 1287	MAGE-3 segment 4	90 nts
SEQ ID NO: 1288	Polypeptide encoded by SEQ ID NO: 1287	30 aa
SEQ ID NO: 1289	MAGE-3 segment 5	90 nts
SEQ ID NO: 1290	Polypeptide encoded by SEQ ID NO: 1289	30 aa
SEQ ID NO: 1291	MAGE-3 segment 6	90 nts
SEQ ID NO: 1292	Polypeptide encoded by SEQ ID NO: 1291	30 aa
SEQ ID NO: 1293	MAGE-3 segment 7	90 nts
SEQ ID NO: 1294	Polypeptide encoded by SEQ ID NO: 1293	30 aa

SEQUENCE ID NUMBER	SIQUENCI	LENGTH
SEQ ID NO: 1295	MAGE-3 segment 8	90 nts
SEQ ID NO: 1296	Polypeptide encoded by SEQ ID NO: 1295	30 aa
SEQ ID NO: 1297	MAGE-3 segment 9	90 nts
SEQ ID NO: 1298	Polypeptide encoded by SEQ ID NO: 1297	30 aa
SEQ ID NO: 1299	MAGE-3 segment 10	90 nts
SEQ ID NO: 1300	Polypeptide encoded by SEQ ID NO: 1299	30 aa
SEQ ID NO: 1301	MAGE-3 segment 11	90 nts
SEQ ID NO: 1302	Polypeptide encoded by SEQ ID NO: 1301	30 aa
SEQ ID NO: 1303	MAGE-3 segment 12	90 nts
SEQ ID NO: 1304	Polypeptide encoded by SEQ ID NO: 1303	30 aa
SEQ ID NO: 1305	MAGE-3 segment 13	90 nts
SEQ ID NO: 1306	Polypeptide encoded by SEQ ID NO: 1305	30 aa
SEQ ID NO: 1307	MAGE-3 segment 14	90 nts
SEQ ID NO: 1308	Polypeptide encoded by SEQ ID NO: 1307	30 aa
SEQ ID NO: 1309	MAGE-3 segment 15	90 nts
SEQ ID NO: 1310	Polypeptide encoded by SEQ ID NO: 1309	30 aa
SEQ ID NO: 1311	MAGE-3 segment 16	90 nts
SEQ ID NO: 1312	Polypeptide encoded by SEQ ID NO: 1311	30 aa
SEQ ID NO: 1313	MAGE-3 segment 17	90 nts
SEQ ID NO: 1314	Polypeptide encoded by SEQ ID NO: 1313	30 aa
SEQ ID NO: 1315	MAGE-3 segment 18	90 nts
SEQ ID NO: 1316	Polypeptide encoded by SEQ ID NO: 1315	30 aa
SEQ ID NO: 1317	MAGE-3 segment 19	90 nts
SEQ ID NO: 1318	Polypeptide encoded by SEQ ID NO: 1317	30 aa

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SIQUENCE ID NUMBER	Sequence :	LINGTH
SEQ ID NO: 1319	MAGE-3 segment 20	90 nts
SEQ ID NO: 1320	Polypeptide encoded by SEQ ID NO: 1319	30 aa
SEQ ID NO: 1321	MAGE-3 segment 21	54 nts
SEQ ID NO: 1322	Polypeptide encoded by SEQ ID NO: 1321	18 aa
SEQ ID NO: 1323	PRAME segment 1	90 nts
SEQ ID NO: 1324	Polypeptide encoded by SEQ ID NO: 1323	30 aa
SEQ ID NO: 1325	PRAME segment 2	90 nts
SEQ ID NO: 1326	Polypeptide encoded by SEQ ID NO: 1325	30 aa
SEQ ID NO: 1327	PRAME segment 3	90 nts
SEQ ID NO: 1328	Polypeptide encoded by SEQ ID NO: 1327	30 aa
SEQ ID NO: 1329	PRAME segment 4 -	90 nts
SEQ ID NO: 1330	Polypeptide encoded by SEQ ID NO: 1329	30 aa
SEQ ID NO: 1331	PRAME segment 5	90 nts
<b>SEQ ID NO: 1332</b>	Polypeptide encoded by SEQ ID NO: 1331	30 aa
<b>SEQ ID NO: 1333</b>	PRAME segment 6	90 nts
SEQ ID NO: 1334	Polypeptide encoded by SEQ ID NO: 1333	30 aa
SEQ ID NO: 1335	PRAME segment 7	90 nts
SEQ ID NO: 1336	Polypeptide encoded by SEQ ID NO: 1335	30 aa
SEQ ID NO: 1337	PRAME segment 8	90 nts
SEQ ID NO: 1338	Polypeptide encoded by SEQ ID NO: 1337	30 aa
SEQ ID NO: 1339	PRAME segment 9	90 nts
SEQ ID NO: 1340	Polypeptide encoded by SEQ ID NO: 1339	30 aa
SEQ ID NO: 1341	PRAME segment 10	90 nts
SEQ ID NO: 1342	Polypeptide encoded by SEQ ID NO: 1341	30 aa

SEQUENCI ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1343	PRAME segment 11	90 nts
SEQ ID NO: 1344	Polypeptide encoded by SEQ ID NO: 1343	30 aa
SEQ ID NO: 1345	PRAME segment 12	90 nts
SEQ ID NO: 1346	Polypeptide encoded by SEQ ID NO: 1345	30 aa
SEQ ID NO: 1347	PRAME segment 13	90 nts
SEQ ID NO: 1348	Polypeptide encoded by SEQ ID NO: 1347	30 aa
SEQ ID NO: 1349	PRAME segment 14	90 nts
SEQ ID NO: 1350	Polypeptide encoded by SEQ ID NO: 1349	30 aa
SEQ ID NO: 1351	PRAME segment 15	90 nts
SEQ ID NO: 1352	Polypeptide encoded by SEQ ID NO: 1351	30 aa
SEQ ID NO: 1353	PRAME segment 16.	90 nts
SEQ ID NO: 1354	Polypeptide encoded by SEQ ID NO: 1353	30 aa
SEQ ID NO: 1355	PRAME segment 17	90 nts
SEQ ID NO: 1356	Polypeptide encoded by SEQ ID NO: 1355	30 aa
SEQ ID NO: 1357	PRAME segment 18	90 nts
SEQ ID NO: 1358	Polypeptide encoded by SEQ ID NO: 1357	30 aa
SEQ ID NO: 1359	PRAME segment 19	90 nts
SEQ ID NO: 1360	Polypeptide encoded by SEQ ID NO: 1359	30 aa
SEQ ID NO: 1361	PRAME segment 20	90 nts
SEQ ID NO: 1362	Polypeptide encoded by SEQ ID NO: 1361	30 aa
SEQ ID NO: 1363	PRAME segment 21	90 nts
SEQ ID NO: 1364	Polypeptide encoded by SEQ ID NO: 1363	30 aa
SEQ ID NO: 1365	PRAME segment 22	90 nts
SEQ ID NO: 1366	Polypeptide encoded by SEQ ID NO: 1365	30 aa

NOVERCE ID NUMBER	LEQUENCE	LENGTH
SEQ ID NO: 1367	PRAME segment 23	90 nts
SEQ ID NO: 1368	Polypeptide encoded by SEQ ID NO: 1367	30 aa
SEQ ID NO: 1369	PRAME segment 24	90 nts
SEQ ID NO: 1370	Polypeptide encoded by SEQ ID NO: 1369	30 aa
SEQ ID NO: 1371	PRAME segment 25	90 nts
SEQ ID NO: 1372	Polypeptide encoded by SEQ ID NO: 1371	30 aa
SEQ ID NO: 1373	PRAME segment 26	90 nts
SEQ ID NO: 1374	Polypeptide encoded by SEQ ID NO: 1373	30 aa
SEQ ID NO: 1375	PRAME segment 27	90 nts
SEQ ID NO: 1376	Polypeptide encoded by SEQ ID NO: 1375	30 aa
SEQ ID NO: 1377	PRAME segment 28	90 nts
SEQ ID NO: 1378	Polypeptide encoded by SEQ ID NO: 1377	30 aa
SEQ ID NO: 1379	PRAME segment 29	90 nts
SEQ ID NO: 1380	Polypeptide encoded by SEQ ID NO: 1379	30 aa
SEQ ID NO: 1381	PRAME segment 30	90 nts
SEQ ID NO: 1382	Polypeptide encoded by SEQ ID NO: 1381	30 aa
SEQ ID NO: 1383	PRAME segment 31	90 nts
SEQ ID NO: 1384	Polypeptide encoded by SEQ ID NO: 1383	30 aa
SEQ ID NO: 1385	PRAME segment 32	90 nts
SEQ ID NO: 1386	Polypeptide encoded by SEQ ID NO: 1385	30 aa
SEQ ID NO: 1387	PRAME segment 33	90 nts
SEQ ID NO: 1388	Polypeptide encoded by SEQ ID NO: 1387	30 aa
SEQ ID NO: 1389	PRAME segment 34	54 nts
SEQ ID NO: 1390	Polypeptide encoded by SEQ ID NO: 1389	18 aa

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SEQUENCI D NUMBER	SEQUENCE.	LENGTH
SEQ ID NO: 1391	TRP2IN2 segment 1	90 nts
SEQ ID NO: 1392	Polypeptide encoded by SEQ ID NO: 1391	30 aa
SEQ ID NO: 1393	TRP2IN2 segment 2	90 nts
SEQ ID NO: 1394	Polypeptide encoded by SEQ ID NO: 1393	30 aa
SEQ ID NO: 1395	TRP2IN2 segment 3	84 nts
SEQ ID NO: 1396	Polypeptide encoded by SEQ ID NO: 1395	28 aa
SEQ ID NO: 1397	NYNSO1a segment 1	90 nts
SEQ ID NO: 1398	Polypeptide encoded by SEQ ID NO: 1397	30 aa
SEQ ID NO: 1399	NYNSO1a segment 2	90 nts
SEQ ID NO: 1400	Polypeptide encoded by SEQ ID NO: 1399	30 aa
SEQ ID NO: 1401	NYNSO1a segment 3	90 nts
SEQ ID NO: 1402	Polypeptide encoded by SEQ ID NO: 1401	30 aa
SEQ ID NO: 1403	NYNSO1a segment 4	90 nts
SEQ ID NO: 1404	Polypeptide encoded by SEQ ID NO: 1403	30 aa
SEQ ID NO: 1405	NYNSO1a segment 5	90 nts
SEQ ID NO: 1406	Polypeptide encoded by SEQ ID NO: 1405	30 aa
SEQ ID NO: 1407	NYNSO1a segment 6	90 nts
SEQ ID NO: 1408	Polypeptide encoded by SEQ ID NO: 1407	30 aa
SEQ ID NO: 1409	NYNSO1a segment 7	90 nts
SEQ ID NO: 1410	Polypeptide encoded by SEQ ID NO: 1409	30 aa
SEQ ID NO: 1411	NYNSO1a segment 8	90 nts
SEQ ID NO: 1412	Polypeptide encoded by SEQ ID NO: 1411	30 aa
SEQ ID NO: 1413	NYNSO1a segment 9	90 nts
SEQ ID NO: 1414	Polypeptide encoded by SEQ ID NO: 1413	30 aa

SIQUINCI ID NUMBIR	SEQUENCE	LENGTH
SEQ ID NO: 1415	NYNSO1a segment 10	90 nts
SEQ ID NO: 1416	Polypeptide encoded by SEQ ID NO: 1415	30 aa
SEQ ID NO: 1417	NYNSO1a segment 11	90 nts
SEQ ID NO: 1418	Polypeptide encoded by SEQ ID NO: 1417	30 aa
SEQ ID NO: 1419	NYNSO1a segment 12	57 nts
SEQ ID NO: 1420	Polypeptide encoded by SEQ ID NO: 1419	19 aa
SEQ ID NO: 1421	NYNSO1b segment 1	90 nts
SEQ ID NO: 1422	Polypeptide encoded by SEQ ID NO: 1421	30 aa
SEQ ID NO: 1423	NYNSO1b segment 2	90 nts
SEQ ID NO: 1424	Polypeptide encoded by SEQ ID NO: 1423	30 aa
SEQ ID NO: 1425	NYNSO1b segment 3	90 nts
SEQ ID NO: 1426	Polypeptide encoded by SEQ ID NO: 1425	30 aa
SEQ ID NO: 1427	NYNSO1b segment 4	51 nts
SEQ ID NO: 1428	Polypeptide encoded by SEQ ID NO: 1427	
SEQ ID NO: 1429	LAGE1 segment 1	90 nts
SEQ ID NO: 1430	Polypeptide encoded by SEQ ID NO: 1429	30 aa
SEQ ID NO: 1431	LAGE1 segment 2	90 nts
SEQ ID NO: 1432	Polypeptide encoded by SEQ ID NO: 1431	30 aa
SEQ ID NO: 1433	LAGE1 segment 3	90 nts
SEQ ID NO: 1434	Polypeptide encoded by SEQ ID NO: 1433	30 aa
SEQ ID NO: 1435	LAGE1 segment 4	90 nts
SEQ ID NO: 1436	Polypeptide encoded by SEQ ID NO: 1435	30 aa
SEQ ID NO: 1437	LAGE1 segment 5	90 nts
SEQ ID NO: 1438	Polypeptide encoded by SEQ ID NO: 1437	30 aa

SEQUENCE ID NUMBER	SIQUENCE.	LENGTH
SEQ ID NO: 1439	LAGE1 segment 6	90 nts
SEQ ID NO: 1440	Polypeptide encoded by SEQ ID NO: 1439	30 aa
SEQ ID NO: 1441	LAGE1 segment 7	90 nts
SEQ ID NO: 1442	Polypeptide encoded by SEQ ID NO: 1441	30 aa
SEQ ID NO: 1443	LAGE1 segment 8	90 nts
SEQ ID NO: 1444	Polypeptide encoded by SEQ ID NO: 1443	30 aa
SEQ ID NO: 1445	LAGE1 segment 9	90 nts
SEQ ID NO: 1446	Polypeptide encoded by SEQ ID NO: 1445	30 aa
SEQ ID NO: 1447	LAGE1 segment 10	90 nts
SEQ ID NO: 1448	Polypeptide encoded by SEQ ID NO: 1447	30 aa
SEQ ID NO: 1449	LAGE1 segment 11	90 nts
SEQ ID NO: 1450	Polypeptide encoded by SEQ ID NO: 1449 30 aa	
SEQ ID NO: 1451	LAGE1 segment 12	57 nts
SEQ ID NO: 1452	Polypeptide encoded by SEQ ID NO: 1451 19 aa	
SEQ ID NO: 1453	Melanoma cancer specific Savine	10623 nts
SEQ ID NO: 1454	Polypeptide encoded by SEQ ID NO: 1453	3541 aa
SEQ ID NO: 1455	Figure 16 A1S1 99mer	99 nts
SEQ ID NO: 1456	Figure 16 A1S2 100mer	100 nts
SEQ ID NO: 1457	Figure 16 A1S3 100mer	100 nts
SEQ ID NO: 1458	Figure 16 A1S4 100mer	100 nts
SEQ ID NO: 1459	Figure 16 A1S5 100mer	100 nts
SEQ ID NO: 1460	Figure 16 A1S6 99mer	99 nts
SEQ ID NO: 1461	Figure 16 A1S7 97mer	99 nts
SEQ ID NO: 1462	Figure 16 A1S8 100mer	100 nts

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SEQUENCE ID NUMBER	STQUENCE	LINGTH
SEQ ID NO: 1463	Figure 16 A1S9 100mer	100 nts
SEQ ID NO: 1464	Figure 16 A1S10 75mer	76 nts
SEQ ID NO: 1465	Figure 16 A1F 20mer	20 nts
SEQ ID NO: 1466	Figure 16 A1R 20mer	20 nts
SEQ ID NO: 1467	Amino acid sequence of immunostimulatory domain of an invasin protein from Yersinia spp.	16 aa

#### DETAILED DESCRIPTION OF THE INVENTION

## 1. Definitions

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The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

As used herein, the term "about" refers to a quantity, level, value, dimension, size, or amount that varies by as much as 30%, preferably by as much as 20%, and more preferably by as much as 10% to a reference quantity, level, value, dimension, size, or amount.

By "antigen-binding molecule" is meant a molecule that has binding affinity for a target antigen. It will be understood that this term extends to immunoglobulins, immunoglobulin fragments and non-immunoglobulin derived protein frameworks that exhibit antigen-binding activity.

The term "clade" as used herein refers to a hypothetical species of an organism and its descendants or a monophyletic group of organisms. Clades carry a definition, based on ancestry, and a diagnosis, based on synapomorphies. It should be noted that diagnoses of clades could change while definitions do not.

Throughout this specification, unless the context requires otherwise, the words "comprise", "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

By "expression vector" is meant any autonomous genetic element capable of directing the synthesis of a protein encoded by the vector. Such expression vectors are known by practitioners in the art.

As used herein, the term "function" refers to a biological, enzymatic, or therapeutic function.

"Homology" refers to the percentage number of amino acids that are identical or constitute conservative substitutions as defined in Table B infra. Homology may be determined using sequence comparison programs such as GAP (Deveraux et al. 1984, Nucleic Acids Research 12, 387-395). In this way, sequences of a similar or substantially different length to those cited herein might be compared by insertion of gaps into the alignment, such gaps being determined, for example, by the comparison algorithm used by GAP.

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To enhance an immune response ("immunoenhancement"), as is well-known in the art, means to increase an animal's capacity to respond to foreign or disease-specific antigens (e.g., cancer antigens) i.e., those cells primed to attack such antigens are increased in number, activity, and ability to detect and destroy the those antigens. Strength of immune response is measured by standard tests including: direct measurement of peripheral blood lymphocytes by means known to the art; natural killer cell cytotoxicity assays (see, e.g., Provinciali M. et al (1992, J. Immunol. Meth. 155: 19-24), cell proliferation assays (see, e.g., Vollenweider, I. and Groseurth, P. J. (1992, J. Immunol. Meth. 149: 133-135), immunoassays of immune cells and subsets (see, e.g., Loeffler, D. A., et al. (1992, Cytom. 13: 169-174); Rivoltini, L., et al. (1992, Can. Immunol. Immunother. 34: 241-251); or skin tests for cell-mediated immunity (see, e.g., Chang, A. E. et al (1993, Cancer Res. 53: 1043-1050). Any statistically significant increase in strength of immune response as measured by the foregoing tests is considered "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein. Enhanced immune response is also indicated by physical manifestations such as fever and inflammation, as well as healing of systemic and local infections, and reduction of symptoms in disease, i.e., decrease in tumour size, alleviation of symptoms of a disease or condition including, but not restricted to, leprosy, tuberculosis, malaria, naphthous ulcers, herpetic and papillomatous warts, gingivitis, artherosclerosis, the concomitants of AIDS such as Kaposi's sarcoma, bronchial infections, and the like. Such physical manifestations response" also define "enhanced immune "immunoenhancement" OI "immunopotentiation" as used herein.

30 Reference herein to "immuno-interactive" includes reference to any interaction, reaction, or other form of association between molecules and in particular where one of the molecules is, or mimics, a component of the immune system.

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By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state.

By "modulating" is meant increasing or decreasing, either directly or indirectly, an immune response against a target antigen of a member selected from the group consisting of a cancer and an organism, preferably a pathogenic organism.

By "natural gene" is meant a gene that naturally encodes a protein.

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The term "natural polypeptide" as used herein refers to a polypeptide that exists in nature.

By "obtained from" is meant that a sample such as, for example, a polynucleotide
extract or polypeptide extract is isolated from, or derived from, a particular source of the
host. For example, the extract can be obtained from a tissue or a biological fluid isolated
directly from the host.

The term "oligonucleotide" as used herein refers to a polymer composed of a multiplicity of nucleotide residues (deoxyribonucleotides or ribonucleotides, or related structural variants or synthetic analogues thereof) linked via phosphodiester bonds (or related structural variants or synthetic analogues thereof). Thus, while the term "oligonucleotide" typically refers to a nucleotide polymer in which the nucleotide residues and linkages between them are naturally occurring, it will be understood that the term also includes within its scope various analogues including, but not restricted to, peptide nucleic acids (PNAs), phosphoramidates, phosphorothioates, methyl phosphonates, 2-O-methyl ribonucleic acids, and the like. The exact size of the molecule can vary depending on the particular application. An oligonucleotide is typically rather short in length, generally from about 10 to 30 nucleotide residues, but the term can refer to molecules of any length, although the term "polynucleotide" or "nucleic acid" is typically used for large oligonucleotides.

By "operably linked" is meant that transcriptional and translational regulatory polynucleotides are positioned relative to a polypeptide-encoding polynucleotide in such a manner that the polynucleotide is transcribed and the polypeptide is translated.

The term "parent polypeptide" as used herein typically refers to a polypeptide encoded by a natural gene. However, it is possible that the parent polypeptide corresponds to a protein that is not naturally-occurring but has been engineered using recombinant techniques. In this instance, a polynucleotide encoding the parent polypeptide may comprise different but synonymous codons relative to a natural gene encoding the same polypeptide. Alternatively, the parent polypeptide may not correspond to a natural polypeptide sequence. For example, the parent polypeptide may comprise one or more consensus sequences common to a plurality of polypeptides.

The term "patient" refers to patients of human or other mammal and includes any individual it is desired to examine or treat using the methods of the invention. However, it will be understood that "patient" does not imply that symptoms are present. Suitable mammals that fall within the scope of the invention include, but are not restricted to, primates, livestock animals (e.g., sheep, cows, horses, donkeys, pigs), laboratory test animals (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., cats, dogs) and captive wild animals (e.g., foxes, deer, dingoes).

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By "pharmaceutically-acceptable carrier" is meant a solid or liquid filler, diluent or encapsulating substance that can be safely used in topical or systemic administration to a mammal.

"Polypeptide", "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues and to variants and synthetic analogues of the same. Thus, these terms apply to amino acid polymers in which one or more amino acid residues is a synthetic non-naturally occurring amino acid, such as a chemical analogue of a corresponding naturally occurring amino acid, as well as to naturally-occurring amino acid polymers.

The term "polynucleotide" or "nucleic acid" as used herein designates mRNA, RNA, cRNA, cDNA or DNA. The term typically refers to oligonucleotides greater than 30 nucleotide residues in length.

By "primer" is meant an oligonucleotide which, when paired with a strand of DNA, is capable of initiating the synthesis of a primer extension product in the presence of a suitable polymerising agent. The primer is preferably single-stranded for maximum

efficiency in amplification but can alternatively be double-stranded. A primer must be sufficiently long to prime the synthesis of extension products in the presence of the polymerisation agent. The length of the primer depends on many factors, including application, temperature to be employed, template reaction conditions, other reagents, and source of primers. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15 to 35 or more nucleotide residues, although it can contain fewer nucleotide residues. Primers can be large polynucleotides, such as from about 35 nucleotides to several kilobases or more. Primers can be selected to be "substantially complementary" to the sequence on the template to which it is designed to hybridise and serve as a site for the initiation of synthesis. By "substantially complementary', it is meant that the primer is sufficiently complementary to hybridise with a target polynucleotide. Preferably, the primer contains no mismatches with the template to which it is designed to hybridise but this is not essential. For example, noncomplementary nucleotide residues can be attached to the 5' end of the primer, with the 15 remainder of the primer sequence being complementary to the template. Alternatively, non-complementary nucleotide residues or a stretch of non-complementary nucleotide residues can be interspersed into a primer, provided that the primer sequence has sufficient complementarity with the sequence of the template to hybridise therewith and thereby form a template for synthesis of the extension product of the primer.

"Probe" refers to a molecule that binds to a specific sequence or sub-sequence or other moiety of another molecule. Unless otherwise indicated, the term "probe" typically refers to a polynucleotide probe that binds to another polynucleotide, often called the "target polynucleotide", through complementary base pairing. Probes can bind target polynucleotides lacking complete sequence complementarity with the probe, depending on the stringency of the hybridisation conditions. Probes can be labelled directly or indirectly.

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By "recombinant polypeptide" is meant a polypeptide made using recombinant techniques, i.e., through the expression of a recombinant or synthetic polynucleotide.

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 monomer

units, inclusive of nucleotides and amino acid residues, in length. Because two polynucleotides may each comprise (1) a sequence (i.e., only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of at least 50 contiguous positions, usually about 50 to about 100, more usually about 100 to about 150 in which a sequence is compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. The comparison window may comprise additions or deletions (i.e., gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerised implementations of algorithms (GAP, 15 BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e., resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul et al., 1997, Nucl. Acids Res. 25:3389. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel et al., "Current Protocols in Molecular Biology", John Wiley & Sons Inc, 1994-1998, Chapter 15.

The term "sequence identity" as used herein refers to the extent that sequences are identical on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, I) or the identical amino acid residue (e.g., Ala, Pro, Ser, Thr, Gly, Val, Leu, Ile, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present

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invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the reference manual accompanying the software.

The term "synthetic polynucleotide" as used herein refers to a polynucleotide formed in vitro by the manipulation of a polynucleotide into a form not normally found in nature. For example, the synthetic polynucleotide can be in the form of an expression vector. Generally, such expression vectors include transcriptional and translational regulatory polynucleotide operably linked to the polynucleotide.

The term "synonymous codon" as used herein refers to a codon having a different nucleotide sequence than another codon but encoding the same amino acid as that other codon.

By "translational efficiency" is meant the efficiency of a cell's protein synthesis machinery to incorporate the amino acid encoded by a codon into a nascent polypeptide chain. This efficiency can be evidenced, for example, by the rate at which the cell is able to synthesise the polypeptide from an RNA template comprising the codon, or by the amount of the polypeptide synthesised from such a template.

By "vector" is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrable with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. A vector system can comprise a single vector or plasmid, two or more vectors or plasmids, which together contain the total DNA to be introduced

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into the genome of the host cell, or a transposon. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. In the present case, the vector is preferably a viral or viral-derived vector, which is operably functional in animal and preferably mammalian cells. Such vector may be derived from a poxvirus, an adenovirus or yeast. The vector can also include a selection marker such as an antibiotic resistance gene that can be used for selection of suitable transformants. Examples of such resistance genes are known to those of skill in the art and include the *nptII* gene that confers resistance to the antibiotics kanamycin and G418 (Geneticin®) and the *hph* gene which confers resistance to the antibiotic hygromycin B.

## 2. Synthetic polypeptides

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The inventors have surprisingly discovered that the structure of a parent polypeptide can be disrupted sufficiently to impede, abrogate or otherwise alter at least one function of the parent polypeptide, while simultaneously minimising the destruction of potentially useful epitopes that are present in the parent polypeptide, by fusing, coupling or otherwise linking together different segments of the parent polypeptide in a different relationship relative to their linkage in the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the resulting synthetic polypeptide is different to a sequence contained within the parent polypeptide. The synthetic polypeptides of the invention are useful as immunopotentiating agents, and are referred to elsewhere in the specification as scrambled antigen vaccines, super attenuated vaccines or "Savines".

Thus, the invention broadly resides in a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

It is preferable but not essential that the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide. For example, in the case of a parent polypeptide that comprises three contiguous or overlapping segments A-B-C-D, these segments may be linked in 23 other possible orders to form a synthetic polypeptide. These orders may be selected from the group consisting of: A-B-D-C, A-C-B-D, A-C-D-B, A-D-B-C, A-D-C-B, B-A-C-D, B-A-D-C, B-C-A-D, B-C-D-A, B-D-A-C, B-D-C-A, C-A-B-D, C-A-D-B, C-B-A-D, C-B-D-A, C-D-B-A, D-A-B-C, D-A-C-B, D-B-A-C, D-B-C-A, D-C-A-B, and D-C-B-A. Although the rearrangement of the segments is preferably random, it is especially preferable to exclude or otherwise minimise rearrangements that result in complete or partial reassembly of the parent sequence (e.g., ADBC, BACD, DABC). It will be appreciated, however, that the probability of such complete or partial reassembly diminishes as the number of segments for rearrangement increases.

The order of the segments is suitably shuffled, reordered or otherwise rearranged relative to the order in which they exist in the parent polypeptide so that the structure of the polypeptide is disrupted sufficiently to impede, abrogate or otherwise alter at least one

function associated with the parent polypeptide. Preferably, the segments of the parent polypeptide are randomly rearranged in the synthetic polypeptide.

The parent polypeptide is suitably a polypeptide that is associated with a disease or condition. For example, the parent polypeptide may be a polypeptide expressed by a pathogenic organism or a cancer. Alternatively, the parent polypeptide can be a self peptide related to an autoimmune disease including, but are not limited to, diseases such as diabetes (e.g., juvenile diabetes), multiple sclerosis, rheumatoid arthritis, myasthenia gravis, atopic dermatitis, and psoriasis and ankylosing spondylitis. Accordingly, the synthetic molecules of the present invention may also have utility for the induction of tolerance in a subject afflicted with an autoimmune disease or condition or with an allergy or other condition to which tolerance is desired. For example tolerance may be induced by contacting an immature dendritic cell of the individual to be treated with a synthetic polypeptide of the invention or by expressing in an immature dendritic cell a synthetic polynucleotide of the invention. Tolerance may also be induced against antigens causing allergic responses (e.g., asthma, hay fever). In this case, the parent polypeptide is suitably an allergenic protein including, but not restricted to, house-dust-mite allergenic proteins as for example described by Thomas and Smith (1998, Allergy, 53(9): 821-832).

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The pathogenic organism includes, but is not restricted to, yeast, a virus, a bacterium, and a parasite. Any natural host of the pathogenic organism is contemplated by the present invention and includes, but is not limited to, mammals, avians and fish. In a preferred embodiment, the pathogenic organism is a virus, which may be an RNA virus or a DNA virus. Preferably, the RNA virus is Human Immunodeficiency Virus (HIV), Poliovirus, and Influenza virus, Rous sarcoma virus, or a Flavivirus such as Japanese encephalitis virus. In a preferred embodiment, the RNA virus is a Hepatitis virus including, but not limited to, Hepatitis strains A, B and C. Suitably, the DNA virus is a Herpesvirus including, but not limited to, Herpes simplex virus, Epstein-Barr virus, Cytomegalovirus and Parvovirus. In a preferred embodiment, the virus is HIV and the parent polypeptide is suitably selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or combination thereof. In an alternate preferred embodiment, the virus is Hepatitis C1a virus and the parent polypeptide is the Hepatitis C1a virus polyprotein.

In another embodiment, the pathogenic organism is a bacterium, which includes, but is not restricted to, *Neisseria* species, *Meningococcal* species, *Haemophilus* species *Salmonella* species, *Streptococcal* species, *Legionella* species and *Mycobacterium* species.

In yet another embodiment, the pathogenic organism is a parasite, which includes, but is not restricted to, *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

Any cancer or tumour is contemplated by the present invention. For example, the cancer or tumour includes, but is not restricted to, melanoma, lung cancer, breast cancer, cervical cancer, prostate cancer, colon cancer, pancreatic cancer, stomach cancer, bladder cancer, kidney cancer, post transplant lymphoproliferative disease (PTLD), Hodgkin's Lymphoma and the like. Preferably, the cancer or tumour relates to melanoma. In a preferred embodiment of this type, the parent polypeptide is a melanocyte differentiation antigen which is suitably selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof. In an alternate preferred embodiment of this type, the parent polypeptide is a melanoma-specific antigen which is suitably selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.

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In a preferred embodiment, the segments are selected on the basis of size. A segment according to the invention may be of any suitable size that can be utilised to elicit an immune response against an antigen encoded by the parent polypeptide. A number of factors can influence the choice of segment size. For example, the size of a segment should be preferably chosen such that it includes, or corresponds to the size of, T cell epitopes and their processing requirement. Practitioners in the art will recognise that class I-restricted T cell epitopes can be between 8 and 10 amino acids in length and if placed next to unnatural flanking residues, such epitopes can generally require 2 to 3 natural flanking amino acids to ensure that they are efficiently processed and presented. Class II-restricted T cell epitopes can range between 12 and 25 amino acids in length and may not require natural flanking residues for efficient proteolytic processing although it is believed that natural flanking residues may play a role. Another important feature of class II-restricted epitopes is that they generally contain a core of 9-10 amino acids in the middle which bind specifically to class II MHC molecules with flanking sequences either side of this core

stabilising binding by associating with conserved structures on either side of class II MHC antigens in a sequence independent manner (Brown et al., 1993). Thus the functional region of class II-restricted epitopes is typically less than 15 amino acids long. The size of linear B cell epitopes and the factors effecting their processing, like class II-restricted epitopes, are quite variable although such epitopes are frequently smaller in size than 15 amino acids. From the foregoing, it is preferable, but not essential, that the size of the segment is at least 4 amino acids, preferably at least 7 amino acids, more preferably at least 12 amino acids, more preferably at least 20 amino acids and more preferably at least 30 amino acids. Suitably, the size of the segment is less than 2000 amino acids, more preferably less than 1000 amino acids, more preferably less than 500 amino acids, more preferably less than 200 amino acids, more preferably less than 100 amino acids, more preferably less than 80 amino acids and even more preferably less than 60 amino acids and still even more preferably less than 40 amino acids. In this regard, it is preferable that the size of the segments is as small as possible so that the synthetic polypeptide adopts a 15 functionally different structure relative to the structure of the parent polypeptide. It is also preferable that the size of the segments is large enough to minimise loss of T cell epitopes. In an especially preferred embodiment, the size of the segment is about 30 amino acids.

An optional spacer may be utilised to space adjacent segments relative to each other. Accordingly, an optional spacer may be interposed between some or all of the segments. The spacer suitably alters proteolytic processing and/or presentation of adjacent segment(s). In a preferred embodiment of this type, the spacer promotes or otherwise enhances proteolytic processing and/or presentation of adjacent segment(s). Preferably, the spacer comprises at least one amino acid. The at least one amino acid is suitably a neutral amino acid. The neutral amino acid is preferably alanine. Alternatively, the at least one amino acid is cysteine.

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In a preferred embodiment, segments are selected such that they have partial sequence identity or homology with one or more other segments. Suitably, at one or both ends of a respective segment there is comprised at least 4 contiguous amino acids, preferably at least 7 contiguous amino acids, more preferably at least 10 contiguous amino acids, more preferably at least 15 contiguous amino acids and even more preferably at least 20 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Preferably, at the or each

end of a respective segment there is comprised less than 500 contiguous amino acids, more preferably less than 200 contiguous amino acids, more preferably less than 100 contiguous amino acids, more preferably less than 50 contiguous amino acids, more preferably less than 40 contiguous amino acids, and even more preferably less than 30 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Such sequence overlap (also referred to elsewhere in the specification as "overlapping fragments" or "overlapping segments") is preferable to ensure potential epitopes at segment boundaries are not lost and to ensure that epitopes at or near segment boundaries are processed efficiently if placed beside or near amino acids that inhibit processing. Preferably, the segment size is about twice the size of the overlap.

In a preferred embodiment, when segments have partial sequence homology therebetween, the homologous sequences suitably comprise conserved and/or non-conserved amino acid differences. Exemplary conservative substitutions are listed in the following table.

### 15 TABLE B

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Original Revidue	Demplery Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn, Gln
Ile ·	Leu, Val
Leu	Ile, Val

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Original Residue	Esimples; Substitutions
Lys	Arg, Gln, Glu
Met	Leu, Ile,
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Туг	Trp, Phe
Val	Ile, Leu

Conserved or non-conserved differences may correspond to polymorphisms in corresponding parent polypeptides. Polymorphic polypeptides are expressed by various pathogenic organisms and cancers. For example, the polymorphic polypeptides may be expressed by different viral strains or clades or by cancers in different individuals.

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Sequence overlap between respective segments is preferable to minimise destruction of any epitope sequences that may result from any shuffling or rearrangement of the segments relative to their existing order in the parent polypeptide. If overlapping segments as described above are employed to form a synthetic polypeptide, it may not be necessary to change the order in which those segments are linked together relative to the order in which corresponding segments are normally present in the parent polypeptide. In this regard, such overlapping segments when linked together in the synthetic polypeptide can adopt a different structure relative to the structure of the parent polypeptide, wherein the different structure does not provide for one or more functions associated with the parent polypeptide. For example, in the case of four segments A-B-C-D each spanning 30 contiguous amino acids of the parent polypeptide and having a 10-amino acid overlapping sequence with one or more adjacent segments, the synthetic polypeptide will have duplicated 10-amino acid sequences bridging segments A-B, B-C and C-D. The presence of these duplicated sequences may be sufficient to render a different structure and to abrogate or alter function relative to the parent polypeptide.

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In a preferred embodiment, segment size is about 30 amino acids and sequence overlap at one or both ends of a respective segment is about 15 amino acids. However, it will be understood that other suitable segment sizes and sequence overlap sizes are contemplated by the present invention, which can be readily ascertained by persons of skill in the art.

It is preferable but not necessary to utilise all the segments of the parent polypeptide in the construction of the synthetic polypeptide. Suitably, at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptide sequence is used in the construction of the synthetic polypeptide. However, it will be understood that the more sequence information from a parent polypeptide that is utilised to construct the synthetic polypeptide, the greater the population coverage will be of the synthetic polypeptide as an immunogen. Preferably, no sequence information from the parent polypeptide is excluded (e.g., because of an apparent lack of immunological epitopes).

Persons of skill in the art will appreciate that when preparing a synthetic polypeptide against a pathogenic organism (e.g., a virus) or a cancer, it may be preferable to use sequence information from a plurality of different polypeptides expressed by the organism or the cancer. Accordingly, in a preferred embodiment, segments from a plurality of different polypeptides are linked together to form a synthetic polypeptide according to the invention. It is preferable in this respect to utilise as many parent polypeptides as possible from, or in relation to, a particular source in the construction of the synthetic polypeptide. The source of parent polypeptides includes, but is not limited to, a pathogenic organism and a cancer. Suitably, at least about 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptides expressed by the source is used in the construction of the synthetic polypeptide. Preferably, parent polypeptides from a virus include, but are not restricted to, latent polypeptides, regulatory polypeptides or polypeptides expressed early during their replication cycle. Suitably, parent polypeptides from a parasite or bacterium include, but are not restricted to, secretory polypeptides and polypeptides expressed on the surface of

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the parasite or bacteria. It is preferred that parent polypeptides from a cancer or tumour are cancer specific polypeptides.

Suitably, hypervariable sequences within the parent polypeptide are excluded from the construction of the synthetic polypeptide.

The synthetic polypeptides of the inventions may be prepared by any suitable procedure known to those of skill in the art. For example, the polypeptide may be synthesised using solution synthesis or solid phase synthesis as described, for example, in Chapter 9 of Atherton and Shephard (1989, Solid Phase Peptide Synthesis: A Practical Approach. IRL Press, Oxford) and in Roberge et al (1995, Science 269: 202). Syntheses may employ, for example, either t-butyloxycarbonyl 9-(t-Boc) fluorenylmethyloxycarbonyl (Fmoc) chemistries (see Chapter 9.1, of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE, John Wiley & Sons, Inc. 1995-1997; Stewart and Young, 1984, Solid Phase Peptide Synthesis, 2nd ed. Pierce Chemical Co., Rockford, Ill; and Atherton and Shephard, supra).

Alternatively, the polypeptides may be prepared by a procedure including the steps of:

- (a) preparing a synthetic construct including a synthetic polynucleotide encoding a synthetic polypeptide wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide, wherein said synthetic polypeptide comprises a plurality of different segments of a parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the parent polypeptide;
  - (b) introducing the synthetic construct into a suitable host cell;
- (c) culturing the host cell to express the synthetic polypeptide from said synthetic construct; and
- (d) isolating the synthetic polypeptide.

The synthetic construct is preferably in the form of an expression vector. For example, the expression vector can be a self-replicating extra-chromosomal vector such as a plasmid, or a vector that integrates into a host genome. Typically, the regulatory polynucleotide may include, but is not limited to, promoter sequences, leader or signal

sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and termination sequences, and enhancer or activator sequences. Constitutive or inducible promoters as known in the art are contemplated by the invention. The promoters may be either naturally occurring promoters, or hybrid promoters that combine elements of more than one promoter. The regulatory polynucleotide will generally be appropriate for the host cell used for expression. Numerous types of appropriate expression vectors and suitable regulatory polynucleotides are known in the art for a variety of host cells.

In a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

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The expression vector may also include a fusion partner (typically provided by the expression vector) so that the synthetic polypeptide of the invention is expressed as a fusion polypeptide with said fusion partner. The main advantage of fusion partners is that they assist identification and/or purification of said fusion polypeptide. In order to express said fusion polypeptide, it is necessary to ligate a polynucleotide according to the invention into the expression vector so that the translational reading frames of the fusion partner and the polynucleotide coincide.

Well known examples of fusion partners include, but are not limited to, glutathione-S-transferase (GST), Fc portion of human IgG, maltose binding protein (MBP) and hexahistidine (HIS6), which are particularly useful for isolation of the fusion polypeptide by affinity chromatography. For the purposes of fusion polypeptide purification by affinity chromatography, relevant matrices for affinity chromatography are glutathione-, amylose-, and nickel- or cobalt-conjugated resins respectively. Many such matrices are available in "kit" form, such as the QIAexpress<sup>TM</sup> system (Qiagen) useful with (HIS6) fusion partners and the Pharmacia GST purification system. In a preferred embodiment, the recombinant polynucleotide is expressed in the commercial vector pFLAG<sup>TM</sup>.

Another fusion partner well known in the art is green fluorescent protein (GFP). This fusion partner serves as a fluorescent "tag" which allows the fusion polypeptide of the invention to be identified by fluorescence microscopy or by flow cytometry. The GFP tag is useful when assessing subcellular localisation of a fusion polypeptide of the invention,

or for isolating cells which express a fusion polypeptide of the invention. Flow cytometric methods such as fluorescence activated cell sorting (FACS) are particularly useful in this latter application. Preferably, the fusion partners also have protease cleavage sites, such as for Factor X<sub>a</sub>, Thrombin and inteins (protein introns), which allow the relevant protease to partially digest the fusion polypeptide of the invention and thereby liberate the recombinant polypeptide of the invention therefrom. The liberated polypeptide can then be isolated from the fusion partner by subsequent chromatographic separation. Fusion partners according to the invention also include within their scope "epitope tags", which are usually short peptide sequences for which a specific antibody is available. Well known examples of epitope tags for which specific monoclonal antibodies are readily available include c-Myc, influenza virus, haemagglutinin and FLAG tags. Alternatively, a fusion partner may be provided to promote other forms of immunity. For example, the fusion partner may be an antigen-binding molecule that is immuno-interactive with a conformational epitope on a target antigen or to a post-translational modification of a target antigen (e.g., an antigen-binding molecule that is immuno-interactive with a glycosylated target antigen).

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The step of introducing the synthetic construct into the host cell may be effected by any suitable method including transfection, and transformation, the choice of which will be dependent on the host cell employed. Such methods are well known to those of skill in the art.

Synthetic polypeptides of the invention may be produced by culturing a host cell transformed with the synthetic construct. The conditions appropriate for protein expression will vary with the choice of expression vector and the host cell. This is easily ascertained by one skilled in the art through routine experimentation.

Suitable host cells for expression may be prokaryotic or eukaryotic. One preferred host cell for expression of a polypeptide according to the invention is a bacterium. The bacterium used may be *Escherichia coli*. Alternatively, the host cell may be an insect cell such as, for example, *SF9* cells that may be utilised with a baculovirus expression system.

The synthetic polypeptide may be conveniently prepared by a person skilled in the art using standard protocols as for example described in Sambrook, *et al.*, MOLECULAR CLONING. A LABORATORY MANUAL (Cold Spring Harbor Press, 1989), in particular

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Sections 16 and 17; Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (John Wiley & Sons, Inc. 1994-1998), in particular Chapters 10 and 16; and Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons, Inc. 1995-1997), in particular Chapters 1, 5 and 6.

The amino acids of the synthetic polypeptide can be any non-naturally occurring or any naturally occurring amino acid. Examples of unnatural amino acids and derivatives during peptide synthesis include but are not limited to, use of 4-amino butyric acid, 6-aminohexanoic acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, t-butylglycine, norleucine, norvaline, phenylglycine, ornithine, sarcosine, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acids contemplated by the present invention is shown in TABLE C.

TABLE C

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. Mon-conventional arrive asid	Non-conventional animo sold
α-aminobutyric acid	L-N-methylalanine
α-amino-α-methylbutyrate	L-N-methylarginine
aminocyclopropane-carboxylate	L-N-methylasparagine
aminoisobutyric acid	L-N-methylaspartic acid
aminonorbornyl-carboxylate	L-N-methylcysteine
cyclohexylalanine	L-N-methylglutamine
cyclopentylalanine	L-N-methylglutamic acid
L-N-methylisoleucine	L-N-methylhistidine
D-alanine	L-N-methylleucine
D-arginine	L-N-methyllysine
D-aspartic acid	L-N-methylmethionine
D-cysteine	L-N-methylnorleucine
D-glutamate	L-N-methylnorvaline
D-glutamic acid	L-N-methylomithine

Non-comvendenal amine sold	Non-comprisonal amino acid
D-histidine	L-N-methylphenylalanine
D-isoleucine	L-N-methylproline
D-leucine	L-N-medlylserine
D-lysine	L-N-methylthreonine
D-methionine	L-N-methyltryptophan
D-ornithine	L-N-methyltyrosine
D-phenylalanine	L-N-methylvaline
D-proline	L-N-methylethylglycine
D-serine	
D-threonine	L-N-methyl-t-butylglycine L-norleucine
D-tryptophan	L-norvaline
D-tyrosine	α-methyl-aminoisobutyrate
D-valine	α-methyl-γ-aminobutyrate
D-α-methylalanine	α-methylcyclohexylalanine
D-α-methylarginine	α-methylcylcopentylalanine
D-α-methylasparagine	α-methyl-α-napthylalanine
D-α-methylaspartate	o-methylpenicillamine
D-a-methylcysteine	N-(4-aminobutyl)glycine
D-α-methylglutamine	N-(2-aminoethyl)glycine
D-α-methylhistidine	N-(3-aminopropyl)glycine
D-α-methylisoleucine	N-amino-α-methylbutyrate
D-α-methylleucine	α-napthylalanine
D-α-methyllysine	N-benzylglycine
D-α-methylmethionine	N-(2-carbamylediyl)glycine
D-α-methylomithiine	N-(carbamylmethyl)glycine

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Non-comunicami cuntro medi	Nen-conventional arrive acid
D-α-methylphenylalanine	N-(2-carboxyethyl)glycine
D-α-methylproline	N-(carboxymethyl)glycine
D-\alpha-methylserine	N-cyclobutylglycine
D-α-methylthreonine	N-cycloheptylglycine
D-α-methyltryptophan	N-cyclohexylglycine
D-α-methyltyrosine	N-cyclodecylglycine
L-a-methylleucine	L-\a-methyllysine
L-α-methylmethionine	L-α-methylnorleucine
L-α-methylnorvatine	L-\alpha-methylornithine
L-α-methylphenylalanine	L-α-methylproline
L-a-methylserine	L-a-methylthreonine
L-o-methyltryptophan	L-a-methyltyrosine
L-a-methylvaline	L-N-methylhomophenylalanine
N-(N-(2,2-diphenylethyl carbamylmethyl)glycine	N-(N-(3,3-diphenylpropyl carbamylmethyl)glycine
1-carboxy-1-(2,2-diphenyl-ethyl amino)cyclopropane	

The invention also contemplates modifying the synthetic polypeptides of the invention using ordinary molecular biological techniques so as to alter their resistance to proteolytic degradation or to optimise solubility properties or to render them more suitable as an immunogenic agent.

# 3. Preparation of synthetic polynucleotides of the invention

The invention contemplates synthetic polynucleotides encoding the synthetic polypeptides as for example described in Section 2 supra. Polynucleotides encoding segments of a parent polypeptide can be produced by any suitable technique. For example, such polynucleotides can be synthesised de novo using readily available machinery.

Sequential synthesis of DNA is described, for example, in U.S. Patent No 4,293,652. Instead of *de novo* synthesis, recombinant techniques may be employed including use of restriction endonucleases to cleave a polynucleotide encoding at least a segment of the parent polypeptide and use of ligases to ligate together in frame a plurality of cleaved polynucleotides encoding different segments of the parent polypeptide. Suitable recombinant techniques are described for example in the relevant sections of Ausubel, *et al.* (*supra*) and of Sambrook, *et al.*, (*supra*) which are incorporated herein by reference. Preferably, the synthetic polynucleotide is constructed using splicing by overlapping extension (SOEing) as for example described by Horton *et al.* (1990, *Biotechniques* 8(5): 528-535; 1995, *Mol Biotechnol.* 3(2): 93-99; and 1997, *Methods Mol Biol.* 67: 141-149). However, it should be noted that the present invention is not dependent on, and not directed to, any one particular technique for constructing the synthetic construct.

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Various modifications to the synthetic polynucleotides may be introduced as a means of increasing intracellular stability and half-life. Possible modifications include but are not limited to the addition of flanking sequences of ribo- or deoxy- nucleotides to the 5' and/or 3' ends of the molecule or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the oligodeoxyribonucleotide backbone.

The invention therefore contemplates a method of producing a synthetic polynucleotide as broadly described above, comprising linking together in the same reading frame at least two nucleic acid sequences encoding different segments of a parent polypeptide to form a synthetic polynucleotide, which encodes a synthetic polypeptide according to the invention. Suitably, nucleic acid sequences encoding at least 10 segments, preferably at least 20 segments, more preferably at least 40 segments and more preferably at least 100 segments of a parent polypeptide are employed to produce the synthetic polynucleotide.

Preferably, the method further comprises selecting segments of the parent polypeptide, reverse translating the selected segments and preparing nucleic acid sequences encoding the selected segments. It is preferred that the method further comprises randomly linking the nucleic acid sequences together to form the synthetic polynucleotide. The nucleic acid sequences may be oligonucleotides or polynucleotides.

Suitably, segments are selected on the basis of size. Additionally, or in the alternative, segments are selected such that they have partial sequence identity or homology (i.e., sequence overlap) with one or more other segments. A number of factors can influence segment size and sequence overlap as mentioned above. In the case of sequence overlap, large amounts of duplicated nucleic acid sequences can sometimes result in sections of nucleic acid being lost during nucleic acid amplification (e.g., polymerase chain reaction, PCR) of such sequences, recombinant plasmid propagation in a bacterial host or during amplification of recombinant viruses containing such sequences. Accordingly, in a preferred embodiment, nucleic acid sequences encoding segments having sequence identity or homology with one or more other encoded segments are not linked together in an arrangement in which the identical or homologous sequences are contiguous. Also, it is preferable that different codons are used to encode a specific amino acid in a duplicated region. In this context, an amino acid of a parent polypeptide sequence is preferably reverse translated to provide a codon which, in the context of adjacent or local 15 sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a duplicated sequence or a palindromic sequence) that is refractory to the execution of a task (e.g., cloning or sequencing). Alternatively, segments may be selected such that they contain a carboxyl terminal leucine residue or such that reverse translated sequences encoding the segments contain restriction enzyme sites for convenient splicing of the reverse translated sequences.

The method optionally further comprises linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids. Such spacer residue(s) may be advantageous in ensuring that epitopes within the segments are processed and presented efficiently. Preferably, the spacer oligonucleotide encodes 2 to 3 spacer residues. The spacer residue is suitably a neutral amino acid, which is preferably alanine.

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Optionally, the method further comprises linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments. Suitably, the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments. Such differences may correspond to polymorphisms as discussed

above. In a preferred embodiment, degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.

When a large number of polymorphisms is intended to be covered, it is preferred that multiple synthetic polynucleotides are constructed rather than a single synthetic polynucleotide, which encodes all variant segments. For example, if there is less than 85% homology between polymorphic polypeptides, then it is preferred that more than one synthetic polynucleotide is constructed.

Preferably, the method further comprises optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell. In this regard, it is well known that the translational efficiency of different codons varies between organisms and that such differences in codon usage can be utilised to enhance the level of protein expression in a particular organism. In this regard, reference may be made to Seed et al. (International Application Publication No WO 96/09378) who disclose the replacement of existing codons in a parent polynucleotide with synonymous codons to enhance expression of viral polypeptides in mammalian host cells. Preferably, the first or second most frequently used codons are employed for codon optimisation.

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Preferably, gene splicing by overlap extension or "gene SOEing" (supra) is employed for the construction of the synthetic polynucleotide which is a PCR-based method of recombining DNA sequences without reliance on restriction sites and of directly generating mutated DNA fragments in vitro. By modifying the sequences incorporated into the 5'-ends of the primers, any pair of PCR products can be made to share a common sequence at one end. Under PCR conditions, the common sequence allows strands from two different fragments to hybridise to one another, forming an overlap. Extension of this overlap by DNA polymerase yields a recombinant molecule. However, a problem with long synthetic constructs is that mutations generally incorporate into amplified products during synthesis. In this instance, it is preferred that resolvase treatment is employed at various steps of the synthesis. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions or mispairing of double stranded DNA and are primarily used by bacteriophages to resolve Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). For example, T7 endonuclease I can be employed in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA. The mutated DNA strands are then hybridised to

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non-mutant or correct DNA sequences, which results in a mispairing of DNA bases. The mispaired bases are recognised by the resolvase, which then cleaves the DNA nearby leaving only correctly hybridised sequences intact. Preferably a thermostable resolvase enzyme is employed during splicing or amplification so that errors are not incorporated in downstream synthesis products.

Synthetic polynucleotides according to the invention can be operably linked to a regulatory polynucleotide in the form a synthetic construct as for example described in Section 2 supra. Synthetic constructs of the invention have utility inter alia as nucleic acid vaccines. The choice of regulatory polynucleotide and synthetic construct will depend on the intended host.

Exemplary expression vectors for expression of a synthetic polypeptide according to the invention include, but are not restricted to, modified Ankara Vaccinia virus as for example described by Allen et al. (2000, J. Immunol. 164(9): 4968-4978), fowlpox virus as for example described by Boyle and Coupar (1988, Virus Res. 10: 343-356) and the herpes simplex amplicons described for example by Fong et al. in U.S. Patent No. 6,051,428. Alternatively, Adenovirus and Epstein-Barr virus vectors, which are preferably capable of accepting large amounts of DNA or RNA sequence information, can be used.

Preferred promoter sequences that can be utilised for expression of synthetic polypeptides include the P7.5 or PE/L promoters as for example disclosed by Kumar and 20 Boyle. (1990, Virology 179: 151-158), CMV and RSV promoters.

The synthetic construct optionally further includes a nucleic acid sequence encoding an immunostimulatory molecule. The immunostimulatory molecule may be fusion partner of the synthetic polypeptide. Alternatively, the immunostimulatory molecule may be translated separately from the synthetic polypeptide. Preferably, the immunostimulatory molecule comprises a general immunostimulatory peptide sequence. For example, the immunostimulatory peptide sequence may comprise a domain of an invasin protein (Inv) from the bacteria *Yersinia* spp as for example disclosed by Brett *et al.* (1993, *Eur. J. Immunol.* 23: 1608-1614). This immune stimulatory property results from the capability of this invasin domain to interact with the β1 integrin molecules present on T cells, particularly activated immune or memory T cells. A preferred embodiment of the invasin domain (Inv) for linkage to a synthetic polypeptide has been previously described

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in U.S. Pat. No. 5,759,551. The said Inv domain has the sequence: Thr-Ala-Lys-Ser-Lys-Lys-Phe-Pro-Ser-Tyr-Thr-Ala-Thr-Tyr-Gln-Phe [SEQ ID NO; 1467] or is an immune stimulatory homologue thereof from the corresponding region in another Yersinia species invasin protein. Such homologues thus may contain substitutions, deletions or insertions of amino acid residues to accommodate strain to strain variation, provided that the homologues retain immune stimulatory properties. The general immunostimulatory sequence may optionally be linked to the synthetic polypeptide by a spacer sequence.

In an alternate embodiment, the immunostimulatory molecule may comprise an immunostimulatory membrane or soluble molecule, which is suitably a T cell costimulatory molecule. Preferably, the T cell co-stimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these. The B7 molecule includes, but is not restricted to, B7-1 and B7-2. Preferably, the B7 molecule is B7-1. Alternatively, the T cell co-stimulatory molecule may be an ICAM molecule such as ICAM-1 and ICAM-2.

In another embodiment, the immunostimulatory molecule can be a cytokine. which includes, but is not restricted to, an interleukin, a lymphokine, tumour necrosis factor and an interferon. Alternatively, the immunostimulatory molecule may comprise an immunomodulatory oligonucleotide as for example disclosed by Krieg in U.S. Patent No. 6,008,200.

Suitably, the size of the synthetic polynucleotide does not exceed the ability of host cells to transcribe, translate or proteolytically process and present epitopes to the immune system. Practitioners in the art will also recognise that the size of the synthetic polynucleotide can impact on the capacity of an expression vector to express the synthetic polynucleotide in a host cell. In this connection, it is known that the efficacy of DNA 25 vaccination reduces with expression vectors greater that 20-kb. In such situations it is preferred that a larger number of smaller synthetic constructs is utilised rather than a single large synthetic construct.

## 4. Immunopotentiating compositions

invention also contemplates composition, comprising a immunopotentiating agent selected from the group consisting of a synthetic polypeptide as 30

described in Section 2, and a synthetic polynucleotide or a synthetic construct as described in Section 3, together with a pharmaceutically acceptable carrier. One or more immunopotentiating agents can be used as actives in the preparation of immunopotentiating compositions. Such preparation uses routine methods known to persons skilled in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredients are often mixed with excipients that are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants that enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminium hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thur-MDP), Nacetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphosphoryloxy)-ethylamine (CGP 1983A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween 80 emulsion. For example, the effectiveness of an adjuvant may be determined by measuring the amount of antibodies resulting from the administration of the composition, wherein those antibodies are directed against one or more antigens presented by the treated cells of the composition.

The immunopotentiating agents may be formulated into a composition as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic basis such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic basis as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

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If desired, devices or compositions containing the immunopotentiating agents suitable for sustained or intermittent release could be, in effect, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body.

The compositions are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

Administration of the gene therapy construct to said mammal, preferably a human, may include delivery via direct oral intake, systemic injection, or delivery to selected tissue(s) or cells, or indirectly via delivery to cells isolated from the mammal or a compatible donor. An example of the latter approach would be stem cell therapy, wherein isolated stem cells having potential for growth and differentiation are transfected with the vector comprising the *Sox18* nucleic acid. The stem cells are cultured for a period and then transferred to the mammal being treated.

With regard to nucleic acid based compositions, all modes of delivery of such compositions are contemplated by the present invention. Delivery of these compositions to cells or tissues of an animal may be facilitated by microprojectile bombardment, liposome mediated transfection (e.g., lipofectin or lipofectamine), electroporation, calcium phosphate or DEAE-dextran-mediated transfection, for example. In an alternate embodiment, a synthetic construct may be used as a therapeutic or prophylactic composition in the form of a "naked DNA" composition as is known in the art. A discussion of suitable delivery methods may be found in Chapter 9 of CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Eds. Ausubel et al.; John Wiley & Sons Inc., 1997 Edition) or on the Internet site DNAvaccine.com. The compositions may be administered by intradermal (e.g., using panjet<sup>TM</sup> delivery) or intramuscular routes.

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The step of introducing the synthetic polynucleotide into a target cell will differ depending on the intended use and species, and can involve one or more of non-viral and viral vectors, cationic liposomes, retroviruses, and adenoviruses such as, for example, described in Mulligan, R.C., (1993 *Science* 260 926-932) which is hereby incorporated by reference. Such methods can include, for example:

- A. Local application of the synthetic polynucleotide by injection (Wolff et al., 1990, Science 247 1465-1468, which is hereby incorporated by reference), surgical implantation, instillation or any other means. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of cells responsive to the protein encoded by the synthetic polynucleotide so as to increase the effectiveness of that treatment. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of another factor or factors required for the activity of said protein.
- B. General systemic delivery by injection of DNA, (Calabretta et al., 1993, Cancer Treat. Rev. 19 169-179, which is incorporated herein by reference), or RNA, alone or in combination with liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference) or any other mediator of delivery. Improved targeting might be achieved by linking the synthetic polynucleotide to a targeting molecule (the so-called "magic bullet" approach employing, for example, an antibody), or by local application by injection, surgical implantation or any other means, of another factor or factors required for the activity of the protein encoding said synthetic polynucleotide, or of cells responsive to said protein.
  - C. Injection or implantation or delivery by any means, of cells that have been modified ex vivo by transfection (for example, in the presence of calcium phosphate: Chen et al., 1987, Mole. Cell Biochem. 7 2745-2752, or of cationic lipids and polyamines: Rose et al., 1991, BioTech. 10 520-525, which articles are incorporated herein by reference), infection, injection, electroporation (Shigekawa et al., 1988, BioTech. 6 742-751, which is incorporated herein by reference) or any other way so as to increase the

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expression of said synthetic polynucleotide in those cells. The modification can be mediated by plasmid, bacteriophage, cosmid, viral (such as adenoviral or retroviral; Mulligan, 1993, Science 260 926-932; Miller, 1992, Nature 357 455-460; Salmons et al., 1993, Hum. Gen. Ther. 4 129-141, which articles are incorporated herein by reference) or other vectors, or other agents of modification such as liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference), or any other mediator of modification. The use of cells as a delivery vehicle for genes or gene products has been described by Barr et al., 1991, Science 254 1507-1512 and by Dhawan et al., 1991, Science 254 1509-1512, which articles are incorporated herein by reference. Treated cells can be delivered in combination with any nutrient, growth factor, matrix or other agent that will promote their survival in the treated subject.

Also encapsulated by the present invention is a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment a therapeutically effective amount of a composition as broadly described above.

The disease or condition may be caused by a pathogenic organism or a cancer as for example described above.

In a preferred embodiment, the immunopotentiating composition of the invention is suitable for treatment of, or prophylaxis against, a cancer. Cancers which could be suitably treated in accordance with the practices of this invention include cancers of the lung, breast, ovary, cervix, colon, head and neck, pancreas, prostate, stomach, bladder, kidney, bone liver, oesophagus, brain, testicle, uterus, melanoma and the various leukemias and lymphomas.

In an alternate embodiment, the immunopotentiating composition is suitable for treatment of, or prophylaxis against, a viral, bacterial or parasitic infection. Viral infections contemplated by the present invention include, but are not restricted to, infections caused by HIV, Hepatitis, Influenza, Japanese encephalitis virus, Epstein-Barr virus and respiratory syncytial virus. Bacterial infections include, but are not restricted to, those caused by Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species. Parasitic

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infections encompassed by the invention include, but are not restricted to, those caused by Plasmodium species, Schistosoma species, Leishmania species, Trypanosoma species, Toxoplasma species and Giardia species.

The above compositions or vaccines may be administered in a manner compatible with the dosage formulation, and in such amount as is therapeutically effective to alleviate patients from the disease or condition or as is prophylactically effective to prevent incidence of the disease or condition in the patient. The dose administered to a patient, in the context of the present invention, should be sufficient to effect a beneficial response in a patient over time such as a reduction or cessation of blood loss. The quantity of the composition or vaccine to be administered may depend on the subject to be treated inclusive of the age, sex, weight and general health condition thereof. In this regard, precise amounts of the composition or vaccine for administration will depend on the judgement of the practitioner. In determining the effective amount of the composition or vaccine to be administered in the treatment of a disease or condition, the physician may 15 evaluate the progression of the disease or condition over time. In any event, those of skill in the art may readily determine suitable dosages of the composition or vaccine of the invention.

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In a preferred embodiment, DNA-based immunopotentiating agent (e.g., 100 µg) is delivered intradermally into a patient at day 1 and at week 8 to prime the patient. A recombinant poxvirus (e.g., at  $10^7$  pfu/mL) from which substantially the same immunopotentiating agent can be expressed is then delivered intradermally as a booster at weeks 16 and 24, respectively.

The effectiveness of the immunisation may be assessed using any suitable technique. For example, CTL lysis assays may be employed using stimulated splenocytes or peripheral blood mononuclear cells (PBMC) on peptide coated or recombinant virus infected cells using 51Cr labelled target cells. Such assays can be performed using for example primate, mouse or human cells (Allen et al., 2000, J. Immunol. 164(9): 4968-4978 also Woodberry et al., infra). Alternatively, the efficacy of the immunisation may be monitored using one or more techniques including, but not limited to, HLA class I Tetramer staining - of both fresh and stimulated PBMCs (see for example Allen et al., supra), proliferation assays (Allen et al., supra), Elispot<sup>TM</sup> Assays and intracellular INF- gamma staining (Allen et al., supra), ELISA Assays - for linear B cell responses; and Western blots of cell sample expressing the synthetic polynucleotides.

## 5. Computer related embodiments

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The design or construction of a synthetic polypeptide sequence or a synthetic polynucleotide sequence according to the invention is suitably facilitated with the assistance of a computer programmed with software, which *inter alia* fragments a parent sequence into fragments, and which links those fragments together in a different relationship relative to their linkage in the parent sequence. The ready use of a parent sequence for the construction of a desired synthetic molecule according to the invention requires that it be stored in a computer-readable format. Thus, in accordance with the present invention, sequence data relating to a parent molecule (e.g., a parent polypeptide) is stored in a machine-readable storage medium, which is capable of processing the data to fragment the sequence of the parent molecule into fragments and to link together the fragments in a different relationship relative to their linkage in the parent molecule.

Therefore, another embodiment of the present invention provides a machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when used by a machine programmed with instructions for using said data, fragments a parent sequence into fragments, and links those fragments together in a different relationship relative to their linkage in the parent sequence. In a preferred embodiment of this type, a machine-readable data storage medium is provided that is capable of reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment and to link together in the same reading frame each of the nucleic acid sequences to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in a parent polypeptide sequence.

In another embodiment, the invention encompasses a computer for designing the sequence of a synthetic polypeptide and/or a synthetic polynucleotide of the invention, wherein the computer comprises wherein said computer comprises: (a) a machine readable data storage medium comprising a data storage material encoded with machine readable data, wherein said machine readable data comprises the sequence of a parent polypeptide; (b) a working memory for storing instructions for processing said machine-readable data;

(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine-readable data into said synthetic polypeptide sequence and/or said synthetic polynucleotide; and (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence and/or said synthetic polynucleotide.

In yet another embodiment, the invention contemplates a computer program product for designing the sequence of a synthetic polynucleotide of the invention, comprising code that receives as input the sequence of a parent polypeptide, code that fragments the sequence of the parent polypeptide into fragments, code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment, code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the parent polypeptide sequence, and a computer readable medium that stores the codes.

A version of these embodiments is presented in Figure 23, which shows a system 10 including a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines 40, all of which are interconnected by a conventional bidirectional system bus 50.

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Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. For example, machine-readable data of this invention may be inputted via the use of a modem or modems 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD. Alternatively, ROM drives or disk drives 24 in conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a synthetic polynucleotide sequence or a synthetic polypeptide sequence as described herein. Output hardware might also include a

printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36.46 coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data processing steps. A number of programs may be used to process the machine readable data of this invention. Exemplary programs may use for example the steps outlined in the flow diagram illustrated in Figure 24. Broadly, these steps include (1) inputting at least one parent polypeptide sequence; (2) optionally adding to alanine spacers at the ends of each polypeptide sequence; (3) fragmenting the polypeptide sequences into fragments (e.g., 30 amino acids long), which are preferably overlapping (e.g., by 15 amino acids); (4) reverse translating the fragment to provide a nucleic acid sequence for each fragment and preferably using for the reverse translation first and second most translationally efficient codons for a cell type, wherein the codons are preferably alternated out of frame with each other in the overlaps of consecutive fragments; (5) randomly rearranging the fragments; (6) checking whether rearranged fragments recreate at least a portion of a parent polypeptide sequence; (7) repeating randomly rearranging the fragments when rearranged fragments recreate said at least a portion; or otherwise (8) linking the rearranged fragments together to produce a synthetic polypeptide sequence and/or a synthetic polynucleotide sequence; and (9) outputting said synthetic polypeptide sequence and/or a synthetic polynucleotide sequence. An example of an algorithm which uses inter alia the aforementioned steps is shown in Figure 25. By way of example, this algorithm has been used for the design of synthetic polynucleotides and synthetic polypeptides according to the present invention for Hepatitis C 1a and for melanoma, as illustrated in Figures 26 and 27.

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Figure 28 shows a cross section of a magnetic data storage medium 100 which can be encoded with machine readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24. The

magnetic domains of coating 102 of medium 100 are polarised or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 23.

Figure 29 shows a cross section of an optically readable data storage medium 110 5 which also can be encoded with such a machine-readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk, which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

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In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarisation of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

In order that the invention may be readily understood and put into practical effect, particular preferred non-limiting embodiments will now be described as follows.

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#### **EXAMPLES**

### EXAMPLE 1

### Preparation of an HIV Savine

### Experimental Protocol

#### 5 Plasmids

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The plasmid pDNAVacc is ampicillin resistant and contains an expression cassette comprising a CMV promoter and enhancer, a synthetic intron, a multiple cloning site (MCS) and a SV40poly A signal sequence (Thomson *et al.*, 1998). The plasmid pTK7.5 and contains a selection cassette, a pox virus 7.5 early/late promoter and a MCS flanked on either side by Vaccinia virus TK gene sequences.

#### Recombinant Vaccinia Viruses

Recombinant Vaccinia viruses expressing the gag, env (IIB) and pol (LAI) genes of HIV-1 were used as previously described and denoted VV-GAG, VV-POL, VV-ENV (Woodberry et al., 1999; Kent et al., 1998).

#### 15 Marker Rescue Recombination

Recombinant Vaccinia viruses containing Savine constructs were generated by marker rescue recombination, using protocols described previously (Boyle *et al.*, 1985). Plaque purified viruses were tested for the TK phenotype and for the appropriate genome arrangement by Southern blot and PCR.

## 20 Oligonucleotides

Oligonucleotides 50 nmol scale and desalted were purchased from Life Technologies. Short oligonucleotides were resuspended in 100  $\mu$ L of water, their concentration determined, then diluted to 20  $\mu$ M for use in PCR or sequencing reactions. Long oligonucleotides for splicing reactions were denatured for 5 minutes at 94°C in 20  $\mu$ L of formamide loading buffer then 0.5  $\mu$ L gel purified on a 6% polyacrylamide gel.

Gel slices containing full-length oligonucleotides were visualised with ethidium bromide, excised, placed in Eppendorf<sup>TM</sup> tubes, combined with 200 μL of water before being crushed using the plunger of a 1 mL syringe. Before being used in splicing reactions the crushed gel was resuspended in an appropriate volume of buffer and 1-2 μL of the resuspendate used directly in the splicing reactions.

## Sequencing

Sequencing was performed using Dye terminator sequencing reactions and analyzed by the Biomedical Resource Facility at the John Curtin School of Medical Research using an ABI automated sequencer.

## 10 Restimulation of Lymphocytes from HIV Infected Patients

Two pools of recombinant Vaccinia viruses containing VV-AC1 + VV-BC1 (Pool 1) or VV-AC2 + VV-BC2 + VV-CC2 (Pool 2) were used to restimulate lymphocytes from the blood samples of HIV-infected patients. Briefly CTL lines were generated from HIV-infected donor PBMC. A fifth of the total PBMC were infected with either Pool 1 or Pool 2 Vaccinia viruses then added back to the original cell suspension. The infected cell suspension was then cultured with IL-7 for 1 week.

## CTL Assays

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Restimulated PBMCs were used as effectors in a standard <sup>51</sup>Cr-release CTL assay. Targets were autologous EBV-transformed lymphoblastoid cell lines (LCLs) infected with the following viruses: Pool 1, Pool 2,VV-GAG, VV-POL or VV-ENV. Assay controls included uninfected targets, targets infected with VV-lacZ (virus control) and K562 cells.

#### Results

## HIV Savine Design

A main goal of the Savine strategy is to include as much protein sequence information from a pathogen or cancer as possible in such a way that potential T cell epitopes remain intact and so that the vaccine or therapy is extremely safe. An HIV Savine is described herein not only to compare this strategy to other strategies but also, to produce

an HIV vaccine that would provide the maximum possible population coverage as well as catering for the major HIV clades.

A number of design criteria was first determined to exploit the many advantages of using a synthetic approach. One advantage is that it is possible to use consensus protein sequences to design these vaccines. Using consensus sequences for a highly variable virus like HTV should provide better vaccine coverage because individual viral isolate sequences may have lost epitopes which induce CTL against the majority of other viral isolates. Thus, using the consensus sequences of each HIV clade rather than individual isolate sequences should provide better vaccine coverage. Taking this one step further, a consensus sequence that covers all HIV clades should theoretically provide better coverage than using just the consensus sequences for individual clades. Before designing such a sequence however, it was decided that a more appropriate and focussed HIV vaccine might be constructed if the various clades were first ranked according to their relative importance. To establish such a ranking the following issues were considered, current prevalence of each clade, the rate at which each clade is increasing and the capacity of various regions of the world to cope with the HIV pandemic (Figures 1 and 2). These criteria produced the following ranking, Clade  $E \ge \text{clade } A > \text{clade } C > \text{clade } B > \text{clade } D > \text{other clades.}$  Clades E and A were considered to almost equal since they are very similar except in their envelope protein sequences, which differ considerably.

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Another advantage of synthesising a designed sequence is that it is possible to incorporate degenerate sequences into their design. In the case of HIV, this means that more than one amino acid can be included at various positions to improve the ability of the vaccine to cater for the various HIV clades and isolates. Coverage is improved because mutations in different HIV clades and also in individual isolate sequences, while mostly destroying specific T cell epitopes, can result in the formation of new potentially useful epitopes nearby (Goulder et al., 1997). Incorporating degenerate amino acid sequences, however, also means that more than one construct must be made and mixed together. The number of constructs required depends on the frequency with which mutations are incorporated into the design. While this approach requires the construction of additional constructs, these constructs can be prepared from the same set of degenerate long oligonucleotides, significantly reducing the cost of providing such considerable interclade coverage.

A set of degeneracy rules was developed for the incorporation of amino acid mutations into the design which meant that a maximum of eight constructs would be required so that theoretically all combinations were present, as follows: 1) Two amino acids at three positions (or less) within any group of nine amino acids (i.e., present in a CTL epitope); 2) Three amino acids at one position and two at another (or not) within any group of nine amino acids; 3) Four amino acids at one position and two at another (or not) within any group of nine amino acids. The reason why these rules were applied to nine amino acids (the average CTL epitope size) and not to larger stretches of amino acid sequence to cater for class II restricted epitopes, is because class II-restricted epitopes generally have a core sequence of nine amino acids in the middle which bind specifically to class II MHC molecules with the extra flanking sequences stabilising binding, by associating with either side of class II MHC antigens in a largely sequence independent manner (Brown et al., 1993).

Using the HIV clade ranking described above, the amino acid degeneracy rules and in some situations the similarity between amino acids, a degenerate consensus protein sequence was designed for each HIV protein using the consensus protein sequences for each HIV clade compiled by the Los Alamos HIV sequence database (Figures 3-11) (HIV Molecular Immunology Database, 1997). It is important to note that in some situations the order with which each of the above design criteria was applied was altered. Each time this 20 was done the primary goal however was to increase the ability of the Savine to cater for interclade differences. Two isolate sequences, GenBank accession U51189 and U46016, for clade E and clade C, respectively, were used when a consensus sequence for some HIV proteins from these two clades was unavailable (Gao et al., 1996; Salminen et al., 1996). The design of a consensus sequence for the hypervariable regions of the HIV envelope protein and in some cases between these regions (hypervariable regions 1-2 and 3-5) was difficult and so these regions were excluded from the vaccine design.

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Once a degenerate consensus sequence was designed for each HIV protein, an approach was then determined for incorporating all the protein sequences safely into the vaccine. One convenient approach to ensure that a vaccine will be safe is to systematically 30 fragment and randomly rearrange the protein sequences together thus abrogating or otherwise altering their structure and function. The protein sequences still have to be immunologically functional however, meaning that the process used to fragment the

sequences should not destroy potential epitopes. To decide on the best approach for systematically fragmenting protein sequences, the main criteria used was the size of T epitopes and their processing requirements. Class I-restricted T cell epitopes are 8-10 amino acids long and generally require 2-3 natural flanking amino acids to ensure their efficient processing and presentation if placed next to unnatural flanking residues (Del Val et al., 1991; Thomson et al., 1995). Class II-restricted T cell epitopes range between 12-25 amino acids long and do appear to require natural flanking residues for processing however, it is difficult to rule out a role for natural flanking residues in all cases due to the complexity of their processing pathways (Thomson et al., 1998). Also class II-restricted epitopes despite being larger than CTL epitopes generally have a core sequence of 9-10 amino acids, which binds to MHC molecules in a sequence specific fashion. Thus, based on current knowledge, it was decided that an advantageous approach was to overlap the fragments by at least 15 amino acids to ensure that potential epitopes which might lie across fragment boundaries are not lost and to ensure that CTL epitopes near fragment boundaries, that are placed beside or near inhibitory amino acids in adjacent fragments, are processed efficiently. In deciding the optimal fragment size, the main criteria used were that size had to be small enough to cause the maximum disruption to the structure and function of proteins but large enough to cover the sequence information as efficiently as possible without any further unnecessary duplication. Based on these criteria the fragments would be twice the overlap size, in this case 30 amino acids long.

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The designed degenerate protein sequences were then separated into fragments 30 amino acid long and overlapping by fifteen amino acids. Two alanine amino acids were also added to the start and end of the first and last fragment for each protein or envelop protein segment to ensure these fragments were not placed directly adjacent to amino acids capable of blocking epitope processing (Del Val et al., 1991). The next step was to reverse translate each protein sequence back into DNA. Duplicating DNA sequences was avoided when constructing DNA sequences encoding a tandem repeat of identical or homologous amino acid sequences to maximise expression of the Savine. In this regard, the first and second most commonly used mammalian codons (shown in Figure 12) were assigned to amino acids in these repeat regions, wherein a first codon was used to encode an amino acid in one of the repeated sequences and wherein a second but synonymous codon was used for the other repeated sequence (e.g., see the gag HIV protein in Figure 13). To cater

for the designed amino acid mutations more than one base was assigned to some positions using the IUPAC DNA codes without exceeding more than three base variations (eight possible combinations) in any group of 27 bases (Figure 12). Where a particular combination of amino acids could not be incorporated, because too many degenerate bases would be required, some or all of the amino acid degeneracy was removed according to the protein consensus design rules outlined above. Also the degenerate codons were checked to determine if they could encode a stop codon, if stop codons could not be avoided then the amino acid degeneracy was also simplified again according to the protein consensus design rules outlined above.

The designed DNA segments were then scrambled randomly and joined to create twenty-two subcassettes approximately 840 bp in size. Extra DNA sequences incorporating sites for one of the cohesive restriction enzymes XbaI, SpeI, AvrII or NheI and 3 additional base pairs (to cater for premature Taq polymerase termination) were then added to each end of each subcassette (Figure 14). Some of these extra DNA sequences also contained, the cohesive restriction sites for SalI or XhoI, Kozak signal sequences and start or stop codons to enable the subcassettes to be joined and expressed either as three large cassettes or one full length protein (Figures 14 and 15).

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In designing the HIV Savine one issue that required investigation was whether such a large DNA molecule would be fully expressed and whether epitopes encoded near the end of the molecule would be efficiently presented to the immune system. The inventors also wished to show that mixing two or more degenerate Savine constructs together could induce T cell responses that recognise mutated sequences. To examine both issues DNA coding for a degenerate murine influenza nucleoprotein CTL epitope, NP365-373, which differs by two amino acids at positions 71 and 72 in influenza strain A/PR/8/34 compared to the A/NT/60/68strain and restricted by H2-Db, was inserted before the last stop codon at the end of the HIV Savine design (Figure 15). An important and unusual characteristic of both of these naturally occurring NP365-373 sequences, which enabled the present inventors to examine the effectiveness of incorporating mutated sequences, is that they generate CTL responses which do not cross react with the alternate sequence (Townsend et. al., 1986). This is an unusual characteristic because epitopes not destroyed by mutation usually induce CTL responses that cross-react.

Up to ten long oligonucleotides up to 100 bases long and two short amplification oligonucleotides were synthesised to enable construction of each subcassette (Life Technologies). In designing each oligonucleotide the 3' end and in most cases also the 5' end had to be either a 'c' or a 'g' to ensure efficient extension during PCR splicing. The overlap region for each long oligonucleotide was designed to be at least 16 bp with approximately 50% G/C content. Also oligonucleotide overlaps were not placed where degenerate DNA bases coded for degenerate amino acids to avoid splicing difficulties later. Where this was too difficult some degenerate bases were removed according to the protein consensus design rules outlined above and indicated in Figure 12. Figure 16 shows an example of the oligonucleotides design for each subcassette.

## Construction of the HIV Savine

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Five of each group of ten designed oligonucleotides were spliced together using stepwise asymmetric PCR (Sandhu et al., 1992) and Splicing by Overlap Extension (SOEing) (Figure 17a). Each subcassette was then PCR amplified, cloned into pBluescript™ II KS<sup>-</sup> using BamHl/EcoRI and 16 individual clones sequenced. Mutations. deletions and insertions were present in the large majority of the clones for each subcassette, despite acrylamide gel purification of the long oligonucleotides. In order to construct a functional Savine with minimal mutations, two clones for each subcassette with no insertions or deletions and hence a complete open reading frame and with minimal numbers of non-designed mutations, were selected from the sixteen available. The subcassettes were then excised from their plasmids and joined by stepwise PCR-amplified ligation using the polymerase blend Elongase<sup>TM</sup> (Life Technology), T4 DNA ligase and the cohesive restriction enzymes Xbal/Spel/AvrII/NheI, to generate two copies of cassettes A, B and C as outlined in Figure 14 and shown in Figure 17b. Predicted sequences for these cassettes are shown in Figure 30. Each cassette was then reamplified by PCR with Elongase™, cloned into pBluescript™ II KS- and 3 of the resulting plasmid clones sequenced using 12 of the 36 sequencing primers designed to cover the full length construct. Clones with minimal or no further mutations were selected for transfer into plasmids for DNA vaccination or used to make recombinant poxviruses. A summary of the 30 number of designed and non-designed mutations in each Savine construct is presented in Table 1.

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TABLE 1
Summary of mutations

8	No. 225	Namber of musicos			
Coramo		Designed	Experied in 2 clones	Actual in 2	િજા-designed
Cassette A	1896	249	124	107	5 (AC1), 8 (AC2)
Cassette B	1184	260	130	124	11 (BC1), 4 (BC2)
Cassette C	1969	276	138	121	10 (CC1), 14 (CC2)
Full length	5742	785	392	352	26 (FL1), 26 (FL2)

Summary of the mutations present in the two full-length clones constructed as determined by sequencing. Includes the number of mutations designed, expected and actually present in the 2 clones and the number of non-designed mutations in each cassette and full-length clone.

# HIV Savine DNA vaccines and Recombinant Vaccinia viruses

To test the immunological effectiveness of the HIV Savine constructs the cassette sequences were transferred into DNA vaccine and poxvirus vectors. These vectors when used either separately in immunological assays described below or together in a 'prime-boost' protocol which has been shown previously to generate strong T cell responses in vivo (Kent et al., 1997).

DNA Vaccination plasmids were constructed by excising the cassettes from the selected plasmid clones with Xbal/XhoI (cassette A) or Xbal/SaII (cassettes B and C) and ligating them into pDNAVacc cut with Xbal/XhoI to create pDVAC1, pDVAC2, pDVBC1, pDVBC2, pDVCC1, pDVCC2, respectively (Figure 18a). These plasmids were then further modified by cloning into their XbaI site a DNA fragment excised using Xbal/AvrII from pTUMERA2 and encoding a synthetic endoplasmic reticulum (ER) signal sequence from the Adenovirus E1A protein (Persson et al., 1980) (Figure 18a). ER signal sequences have been shown previously to enhance the presentation of both CTL and T helper epitopes in vivo (Ishioka, G.Y., 1999; Thomson et al., 1998). The plasmids pDVERAC1, pDVERBC1, pDVERCC1 andpDVERAC2, pDVERBC2, pDVERCC2 were then mixed

together to create, plasmid pool 1 and pool 2 respectively. Each plasmid pool collectively encodes one copy of the designed full-length HIV Savine.

Plasmids to generate recombinant Vaccinia viruses which express HIV Savine sequences were constructed by excising the various HIV Savine cassettes from the selected plasmid clones using BamHI/XhoI (cassette A) or BamHI/SaII (cassettes B and C) and cloned into the marker rescue plasmid, pTK7.5, cleaved with BamHI/SalI. These pTK7.5derived plasmids were then used to generate recombinant Vaccinia viruses by marker rescue recombination using established protocols (Boyle et al., 1985) to generate VV-AC1, VV-AC2, VV-BC1, VV-BC2, VV-CC1 and VV-CC2 (Figure 18b).

Two further DNA vaccine plasmids were constructed each encoding a version of the full length HIV Savine (Figure 18c). Briefly, the two versions of cassette B were excised with XhoI and cloned into the corresponding selected plasmid clones containing cassette A sequences that were cut with XhoI/SalI to generate pBSAB1 and pBSAB2 respectively. The joined A/B cassettes in pBSAB1 and pBSAB2 were excised with 15 Xbal/XhoI and cloned into pDVCC1 and pDVCC2, respectively, and cleaved with Xbal/XhoI to generate pDVFL1 and pDVFL2. These were then further modified to contain an ER signal sequence using the same cloning strategy as outlined in figure 18a.

#### Restimulation of HIV specific lymphocytes from HIV infected patients

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The present inventors examined the capacity of the HIV Savine to restimulate HIV-specific polyclonal CTL responses from HIV-infected patients, PBMCs from three different patients were restimulated in vitro with two HIV Savine Vaccinia virus pools (Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2) then used in CTL lysis assays against LCLs infected either with one of the Savine Vaccinia virus pools or Vaccinia viruses which express gag, env or pol. Figure 19 clearly shows, 25 that in all three assays, both HIV Savine viral pools restimulated HIV-specific CTL responses which could recognise targets expressing whole natural HIV antigens and not targets which were uninfected or infected with the control Vaccinia virus. Furthermore, in all three cases, both pools restimulated responses that recognised all three natural HIV antigens. This result suggests that the combined Savine constructs will provide broader 30 immunological coverage than single antigen based vaccine approaches. The level of lysis in each case of targets infected with Savine viral pools was significantly higher than the

lysis recorded for any other infected target. This probably reflects the combined CTL responses to gag, pol, and env plus other HIV antigens not analysed here but whose sequences are also incorporated into the Savine constructs.

CTL recognition of each HIV antigen is largely controlled by each patient's HLA background hence the pattern of CTL lysis for whole HIV antigens is different in each patient. Interestingly, this CTL lysis pattern did not change when the second Savine Vaccinia virus pool was used for CTL restimulation. In these assays, therefore, the inventors were unable to demonstrate clear differences between pools 1 and 2, despite pool 1 lacking a Vaccinia virus expressing cassette CC1 and despite the many amino acid differences between the A and B cassettes in each pool (see table 1).

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From the foregoing, the present inventors have developed a novel vaccine/therapeutic strategy. In one embodiment, pathogen or cancer protein sequences are systemically fragmented, reverse translated back into DNA, rearranged randomly then joined back together. The designed synthetic DNA sequence is then constructed using long oligonucleotides and can be transferred into a range of delivery vectors. The vaccine vectors used here were DNA vaccine plasmids and recombinant poxvirus vectors which have been previously shown to elicit strong T cell responses when used together in a 'prime-boost' protocol (Kent et al., 1997). An important advantage of scrambled antigen vaccines or 'Savines' is that the amount of starting sequence information for the design can be easily expanded to include the majority of the protein sequences from a pathogen or for cancer, thereby providing the maximum possible vaccine or therapy coverage for a given population.

An embodiment of the systematic fragmentation approach described herein was based on the size and processing requirements for T cell epitopes and was designed to cause maximal disruption to the structure and function of protein sequences. This fragmentation approach ensures that the maximum possible range of T cell epitopes will be present from any incorporated protein sequence without the protein being functional and able to compromise vaccine safety

Another important advantage of Savines is that consensus protein sequences can be used for their design. This feature is only applicable when the design needs to cater for pathogen or cancer antigens whose sequence varies considerably. HIV is a highly

mutagenic virus, hence this feature was utilised extensively to design a vaccine which has the potential to cover not only field isolates of HIV but also the major HIV clades involved in the current HIV pandemic. To construct the HIV Savine, one set of long oligonucleotides was synthesised, which included degenerate bases in such a way that 8 constructs are theoretically required for the vaccine to contain all combinations in any stretch of 9 amino acids. The inventors believe that this approach can be improved for the following reasons: 1) While degenerate bases should be theoretically equally represented, in practice some degenerate bases were biased towards one base or the other, leading to a lower than expected frequency of the designed mutations in the two full length HIV Savines which were constructed (see Table 1). 2) Only sequence combinations actually present in the HIV clade consensus sequences are required to get full clade coverage, hence the number of full length constructs needed could be reduced. To reduce the number of constructs however, separate sets of long oligonucleotides would have to be synthesised, significantly increasing the cost, time and effort required to generate a vaccine capable of such considerable vaccine coverage.

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A significant problem during the construction of the HIV Savine synthetic DNA sequence was the incorporation of non-designed mutations. The most serious types of mutations were insertions, deletions or those giving rise to stop codons, all of which change the frame of the synthesised sequences and/or caused premature truncation of the Savine proteins. These types of mutation were removed during construction of the HIV Savines by sequencing multiple clones after subcassette and cassette construction and selecting functional clones. The major source of these non-designed mutations was in the long oligonucleotides used for Savine synthesis, despite their gel purification. This problem could be reduced by making the initial subcassettes smaller thereby reducing the possibility of corrupted oligonucleotides being incorporated into each subcassette clone. The second major cause of non-designed mutations was the large number of PCR cycles required for the PCR and ligation-mediated joining of the subcassettes. Including extra sequencing and clone selection steps during the subcassette joining process should help to reduce the frequency of non-designed mutations in future constructs. Finally, another method that could help reduce the frequency of such mutations at all stages is to use resolvase treatment. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions to double stranded DNA and are primarily used by bacteriophages to resolve

Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). T7 endonuclease I has already been used by the present inventors in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA to allow gel purification of correct sequences. Cleavage of corrupted sequences occurs because after a simple denaturing and hybridisation step mutated DNA hybridises to correct DNA sequences and results in a mispairing of DNA bases which is able to be recognised by the resolvase. This method resulted in a 50% reduction in the frequency of errors. Further optimisation of this method and the use of a thermostable version of this type of enzyme could further reduce the frequency of errors during long Savine construction.

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Two pools of Vaccinia viruses expressing Savine cassettes were both shown to restimulate HIV-specific responses from three different patients infected with B clade HIV viruses. These results provide a clear indication that the HIV Savine should provide broad coverage of the population because each patient had a different HLA pattern yet both pools were able to restimulate HIV-specific CTL responses in all three patients against all three 15 natural HIV proteins tested. Also, both pools were shown to restimulate virtually identical CTL patterns in all three patients. This result was unexpected because some responses should have been lost or gained due to the amino acid differences between the two pools and because Pool 1 is only capable of expressing 2/3 of the full length HIV Savine. There are two suggested reasons why the pattern of CTL lysis was not altered between the two 20 viral pools. Firstly, the sequences in the Savine constructs are nearly all duplicated because the fragment sequences overlap. Hence the loss of a third of the Savine may not have excluded sufficient T cell epitopes for differences to be detected in only three patient samples against only three HIV proteins. Secondly, while mutations often destroy T cell epitopes, if they remain functional, then the CTL they generate frequently can recognise alternate epitope sequences. Taken together this finding indirectly suggests that combining only two Savine constructs may provide robust multiclade coverage. Further experiments are being carried out to directly examine the capacity of the HIV Savine to stimulate CTL generated by different strains of HIV virus. The capacity of the two HIV-1 Savine Vaccinia vector pools to stimulate CD4+ T cell HIV-1 specific responses from infected patients was also tested (Figure 20). Both patients showed significant proliferation of CD4+ T cells although both pools did not show consistent patterns suggesting that the two pools may provide wider vaccine coverage than using either pool independently.

The present inventors have generated a novel vaccine strategy, which has been used to generate what the inventors believe to be the most effective HIV candidate vaccine to date. The inventors have used this vaccine to immunise naive mice. Figure 21 shows conclusively that the HIV-1 Savine described above can generate a Gag and Nef CTL response in naïve mice. It should be noted, however, that the Nef CTL epitope appeared to exist only in Pool 1 since it was not restimulated by Pool 2. This is further proof of the utility of combining HIV-1 Savine Pool 1 and Pool 2 components together to provide broader vaccine coverage.

The HIV-1 Savine Vaccinia vectors have also been used to restimulate in vivo HIV-1 responses in pre-immune M. nemestrina monkeys. These experiments (Figure 22) showed, by INF-γ ELISPOT and CD69 expression on both CD4 and CD8 T cells, that the ability of the HIV-1 SAVINE to restimulate HIV-1 specific responses in vivo is equivalent or perhaps better than another HIV-1 candidate vaccine.

This is a generic strategy able to be applied to many other human infections or cancers where T-cell responses are considered to be important for protection or recovery. With this in mind the inventors have begun constructing Savines for melanoma, cervical cancer and Hepatitis C. In the case of melanoma, the majority of the currently identified melanoma antigens have been divided into two groups, one containing antigens associated with melanoma and one containing differentiation antigens from melanocytes, which are often upregulated in melanomas. Two Savine constructs are presently being constructed to cater for these two groups. The reason for making the distinction is that treatment of melanoma might first proceed using the Savine that incorporates fragments of melanoma specific antigens only. If this Savine fails to control some metastases then the less specific Savine containing the melanocyte-specific antigens can then be used. It is important to point out that other cancers also express many of the antigens specific to melanomas e.g., testicular and breast cancers. Hence the melanoma specific Savine may have therapeutic benefits for other cancers.

A small Savine is also being constructed for cervical cancer. This Savine will contain two antigens, E6 and E7, from two strains of human papilloma virus (HPV), HPV
16 and HPV-18, directly linked with causing the majority of cervical cancers worldwide.

There is a large number of sequence differences in these two antigens between the two

strains which would normally require two Savines to be constructed. However since this Savine is small, the antigen fragments from both strains are being scrambled together. While it is normally better for the Savine approach to include all or a majority of the antigens from a virus, in this case only E6 and E7 are expressed during viral latency or in cervical carcinomas. Hence in the interests of simplicity, the rest of the HPV genome will not be included although all HPV antigens would be desirable in a Savine against genital warts.

Two Savines have also been constructed for two strains of hepatitis C, a major cause of liver disease in the world. Hepatitis C is similar to HIV in the requirements for a vaccine or therapeutic. However, the major hepatitis C strains share significantly lower homology, 69-79%, with one another than do the various HIV clades. To cater for this the inventors have decided to construct two separate constructs to cater for the two major strains present in Australia, types 1 aand 3a, which together cause approximately 80-95% of hepatitis C infections in this country. Both constructs will be approximately the same size as the HIV Savine but will be blended together into a single vaccine or therapy.

Overall it is believed that the Savine vaccine strategy is a generic technology likely to be applied to a wide range of human diseases. It is also believed that because it is not necessary to characterise each antigen, this technology will be actively applied to animal vaccines as well where research into vaccines or therapies is often inhibited by the lack of specific reagents, modest research budgets and poor returns on animal vaccines.

#### **EXAMPLE 2**

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#### Hepatitis C Savine

Synthetic immunomodulatory molecules have also been designed for treating Hepatitis C. In one example, the algorithm of Figure 25 was applied to a consensus polyprotein sequence of Hepatitis C 1a to facilitate its segmentation into overlapping segments (30 aa segments overlapping by 15 aa), the rearrangement of these segments into a scrambled order and the output of Savine nucleic acid and amino acid sequences, as shown in Figure 26. Exemplary DNA cassettes (A, B and C) are also shown in Figure 26, which contain suitable restriction enzyme sites at their ends to facilitate their joining into a single expressible open reading frame.

## **EXAMPLE 3**

### Melanoma Savine

The algorithm of Figure 25 was also applied to melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1), as shown in Figure 27, to provide separate Savine nucleic acid and amino acid sequences for treating or preventing melanoma.

#### **EXAMPLE 4**

## Resolvase Repair Experiment

A resolvase can be used advantageously to repair errors in polynucleotides. The following procedure outlines resolvase repair of a synthetic 340 bp fragment in which DNA errors were common.

## <u>Method</u>

The 340 bp fragment was PCR amplified and gel purified on a 4% agarose gel. After spin purifying, 10ul of the eluate corresponding to approximately 100 ng was subjected to the resolvase repair treatment. The rest of the DNA sample was stored for later cloning as the untreated control.

2 μL of 10xPCR buffer, 2 μL of 20 mM MgCl<sub>2</sub> and 6 μL of MilliQ<sup>TM</sup> water (MQW) and Taq DNA polymerase were added to the 10 μL DNA sample. The mixture was subjected to the following thermal profile; 95°C for 5min, 65°C for 30min, cooled and held at 37°C. Five μL of 10xT7 endonuclease I buffer, 8 μL of 1/50 μL of T7endoI enzyme stock and 17 μL of MQW were added, mixed and incubated for 30 min. Loading buffer was added to the sample and the sample was electrophoresed on a 4% agarose gel. A faint band corresponding to the full length fragment was excised and subjected to 15 further cycles of PCR. The amplified fragment was agarose gel purified and, along with the untreated DNA sample, cloned into pBluescript. Eleven plasmid clones for each DNA sample were sequenced and the number and type of errors compared (see table)

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Buffers were as follows:

## 10x T7endonuclease buffer

2.5ml 1M TRIS pH7.8, 0.5ml 1M MgCl<sub>2</sub>, 25  $\mu$ L 1 M DTT, 50  $\mu$ L 10mg/mL BSA, 2 mL MQW made up to a total of 5 mL.

## 5 T7 endonuclease I stock

Concentrated sample of enzyme prepared by, and obtained from, Jeff Babon (St Vincent's Hospital) was diluted 1/50 using the following dilution buffer: 50  $\mu$ L 1 M TRIS pH7.8, 0.1 $\mu$ L 1M EDTA pH8, 5  $\mu$ L 100 mM glutathione, 50  $\mu$ L 10mg/mL BSA, 2.3 mL MQW, 2.5 mL glycerol made up to a total of 5 mL.

## 10 Results

The results are summarised in Tables 2 and 3.

TABLE 2

Total Ecrors				
. Utilizated	Resolvene treated			
A/T to $G/C = 6$	A/T to G/C = 1			
G/C to A/T = 12	G/C to A/T = 7			
A/T to deletion = 1	A/T to deletion = 1			
G/C to deletion = 6	G/C to deletion = 3			

TABLE 3

Chae summary				
Utersaced	Resolving tremed			
6/11 contained deletions	3/11 contained deletions			

Clone surrery				
Untend	Resolvane breated			
2/11 correct	3/11 correct			

## Discussion/Conclusion

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While overall the number of correct clones obtained was not significantly different, there was a significant difference in the level of errors. This reduction in errors becomes more significant as greater numbers of long oligonucleotides are joined into the one construct *i.e.*, increasing the difference between untreated *versus* treated samples in the chance of obtaining a correct clone. It is believed that combining another resolvase such as T4 endonuclease VII may further enhance repair or increase the bias against errors.

Importantly, this experiment was not optimised e.g., by using proofreading PCR enzymes or optimised conditions. Finally if the repair reaction is carried out during normal PCR, for example, by including a thermostable resolvase, it is believed that amplification of already damaged long oligonucleotides, and the normal accumulation of PCR induced errors, even using error reading polymerases during PCR, could be reduced significantly. The repair of damaged long oligonucleotides is particularly important for synthesis of long DNA fragment such as in Savines because, while the rate of long oligonucleotide damage is typically <5%, after joining 10 oligonucleotides, the error rate approaches 50%. This is true even using the best proofreading PCR enzymes because these enzymes do not verify the sequence integrity using correct oligonucleotide templates that exist as a significant majority (95%) in a joining reaction.

The disclosure of every patent, patent application, and publication cited herein is incorporated herein by reference in its entirety.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in

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light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the appended claims.

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### WHAT IS CLAIMED IS:

- 1. A synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 2. The synthetic polypeptide of claim 1, consisting essentially of different segments of a single parent polypeptide.
- 3. The synthetic polypeptide of claim 1, consisting essentially of different segments of a plurality of different parent polypeptides.
- 4. The synthetic polypeptide of claim 1, wherein the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to their linkage in said at least one parent polypeptide.
- 5. The synthetic polypeptide of claim 4, wherein the segments in said synthetic polypeptide are randomly rearranged relative to their order or arrangement in said at least one parent polypeptide.
- 6. The synthetic polypeptide of claim 1, wherein the size of an individual segment is at least 4 amino acids.
- 7. The synthetic polypeptide of claim 6, wherein the size of an individual segment is from about 20 to about 60 amino acids.
- 8. The synthetic polypeptide of claim 7, wherein the size of an individual segment is about 30 amino acids.
- 9. The synthetic polypeptide of claim 7, comprising at least 30% of the parent polypeptide sequence.
- 10. The synthetic polypeptide of claim 1, wherein at least one of said segments comprises partial sequence identity or homology to one or more other said segments.
- 11. The synthetic polypeptide of claim 10, wherein the sequence identity or homology is contained at one or both ends of an individual segment.

- 12. The synthetic polypeptide of claim 11, wherein one or both ends of said segment comprises at least 4 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments.
- 13. The synthetic polypeptide of claim 10, wherein the size of an individual segment is about twice the size of the sequence that is identical or homologous to the or each other said segment.
- 14. The synthetic polypeptide of claim 13, wherein the size of an individual segment is about 30 amino acids and the size of the sequence that is identical or homologous to the or each other said segment is about 15 amino acids.
- 15. The synthetic polypeptide of claim 1, wherein an optional spacer is interposed between some or all of the segments.
- 16. The synthetic polypeptide of claim 15, wherein the spacer alters proteolytic processing and/or presentation of adjacent segment(s).
- 17. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one neutral amino acid.
- 18. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one alanine residue.
- 19. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is associated with a disease or condition.
- 20. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is selected from a polypeptide of a pathogenic organism, a cancer-associated polypeptide, an autoimmune disease-associated polypeptide, an allergy-associated polypeptide or a variant or derivative of these.
- 21. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a polypeptide of a virus.
- 22. The synthetic polypeptide of claim 21, wherein the virus is selected from a Human Immunodeficiency Virus (HIV) or a Hepatitis virus.
- 23. The synthetic polypeptide of claim 22, wherein the virus is a Human Immunodeficiency Virus (HIV) and the at least one parent polypeptide is selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or a combination thereof.

- 24. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a cancer-associated polypeptide.
- 25. The synthetic polypeptide of claim 24, wherein the cancer is melanoma.
- 26. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen.
- 27. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof.
- 28. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen.
- 29. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.
- 30. A synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 31. A method for producing the synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said method comprising:
  - linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of the at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.
- 32. The method of claim 31, further comprising fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in a respective parent polypeptide sequence.

- 33. The method of claim 32, wherein the fragments are randomly linked together.
- 34. The method of claim 31, further comprising reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment.
- 35. The method of claim 34, wherein an amino acid of a respective parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 36. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.
- 37. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence selected from a palindromic sequence or a duplicated sequence, which is refractory to the execution of a task selected from cloning or sequencing.
- 38. The method of claim 31, further comprising linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids.
- 39. The method of claim 38, wherein spacer oligonucleotide encodes 2 to 3 spacer residues.
- 40. The method of claim 38 or claim 39, wherein the spacer residue is a neutral amino acid.
- 41. The method of claim 38 or claim 39, wherein the spacer residue is alanine.
- 42. The method of claim 31, further comprising linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments.

- 43. The method of claim 42, wherein the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments.
- 44. The method of claim 43, wherein the differences correspond to sequence polymorphisms.
- 45. The method of claim 44, wherein degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.
- 46. The method of claim 31, further comprising optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell.
- 47. A synthetic construct comprising a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide.
- 48. The synthetic construct of claim 47, further including a nucleic acid sequence encoding an immunostimulatory molecule.
- 49. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises a domain of an invasin protein (Inv).
- 50. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises the sequence set forth in SEQ ID NO: 1467 or an immune stimulatory homologue thereof.
- 51. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule.
- 52. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule selected from a B7 molecule or an ICAM molecule.
- 53. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these.

- 54. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a cytokine selected from an interleukin, a lymphokine, tumour necrosis factor or an interferon.
- 55. The synthetic construct of claim 48, wherein the immunostimulatory molecule is an immunomodulatory oligonucleotide.
- 56. An immunopotentiating composition, comprising an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30 or the synthetic construct of claim 47, together with a pharmaceutically acceptable carrier.
- 57. The composition of claim 56, further comprising an adjuvant.
- 58. A method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 59. A method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 60. A computer program product for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said program product comprising:
  - code that receives as input the sequence of said at least one parent polypeptide;
  - code that fragments the sequence of a respective parent polypeptide into fragments;
  - code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and

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- a computer readable medium that stores the codes.
- 61. The computer program product of claim 60, further comprising code that randomly rearranges said fragments.
- 62. The computer program product of claim 60, further comprising code that links the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.
- 63. A computer program product for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, comprising:
  - code that receives as input the sequence of at least one parent polypeptide;
  - code that fragments the sequence of a respective parent polypeptide into fragments;
  - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
  - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
    - a computer readable medium that stores the codes.
- 64. The computer program product of claim 63, further comprising code that randomly rearranges said nucleic acid sequences.
- 65. The computer program product of claim 64, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 66. The computer program product of claim 63, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon

which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

- 67. The computer program product of claim 63, further comprising code that links a spacer oligonucleotide to one or more of said nucleic acid sequences.
- 68. A computer for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
  - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
  - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.
- 69. The computer of claim 68, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.
- 70. The computer of claim 68, wherein the processing of said machine readable data comprises randomly rearranging said fragments.
- 71. The computer of claim 68, wherein the processing of said machine readable data comprises linking the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.

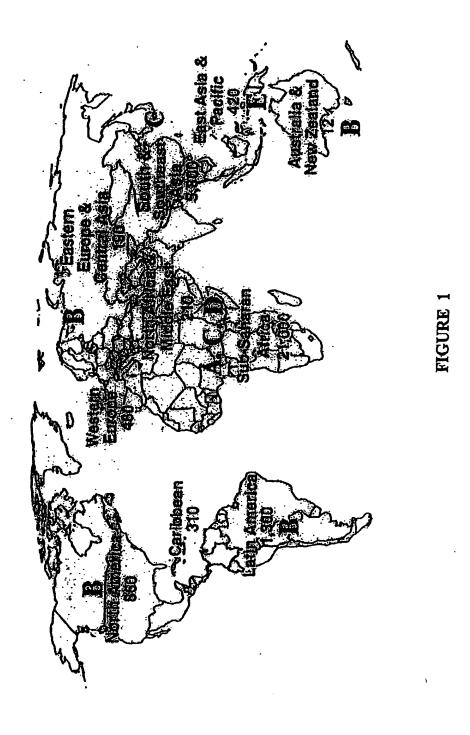
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- 72. A computer for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
  - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
  - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.
- 73. The computer of claim 72, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.
- 74. The computer of claim 72, wherein the processing of said machine readable data comprises randomly rearranging said nucleic acid sequences.
- 75. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.

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76. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

77. The computer of claim 72, wherein the processing of said machine readable data comprises linking a spacer oligonucleotide to one or more of said nucleic acid sequences.



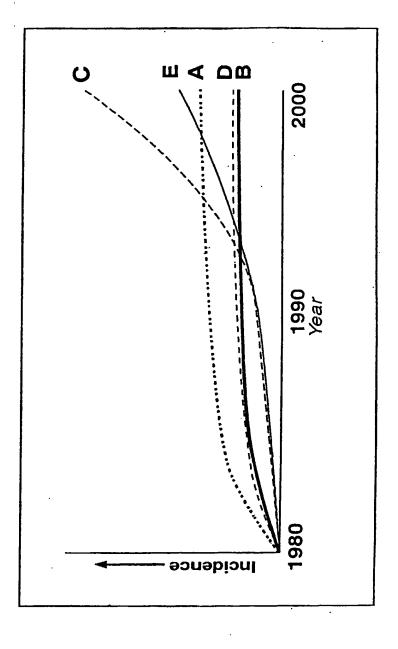


FIGURE 2

/<nls membrane binding designed seq mgarasvlsggkldawekirlrpggkkky<u>k</u>mkhlvwasrelerpalnpglletabgcqqilbqlqsalkt 70 S K G P Q MUTATED AAS mgarasvi.sggki.daneki.rl.rpggkkkykmkhlvwasrelerfalnpgli.etaegcqqli.eqlqstlkt K-ISOLATE 70 mGARaSvLsggkLDawekIrLRPgGkKkYrlKHlvwAsreLerFaLnPslLeTaegcqqimeQlqsalkT 70 CONSENSUS-A -----i-r----?-----h-Mi-------g---s--k--ik---P--Q-CONSENSUS-B 70 69 CONSENSUS-C ------G---s--k--ig---P-ig-CONSENSUS-D 68 -----i--g---s---rk-Ig---ps-Q-CONSENSUS-F 70 63 64 62 42 /<- nls ->/ DESIGNED SEQ GSEELKSLYNTIATLWCVHORIEVKDTKEALDKIEEEOKKSQQK......TQQAAA..DT.GS...SSKV ·VNK MUTATED AAS TRFV GSEELKSLYNTIATLWCVHQRIEVKDTKEALDKIEEVQKKSQQKK.....QQAAA..DT.GS...SSKV R-ISOLATE g?eElkSLfNtvatLycvHqrIdvkDtKeAldkiEeignKskqk?????tqqaaA..?T.gs?..sskv 126 CONSENSUS-A 128 120 CONSENSUS-C 125 CONSENSUS-D 123 CONSENSUS-F 110 CONSENSUS-G CONSENSUS-H 106 106 CONSENSUS-O CONSENSUS-CPZ 2S????----??V-W-?-???????--??-???K??????Q??T-S---???G????-????-??????? 61 p17 \/ p24 DESIGNED SEQ ....SONYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNHMLNIVGGH MUTATED AAS AS .... SQNYPIVQNAQCQMVHQPLSPRTLNANVKVIEEKGPNPEVIPMFSALSEGATPQDLNMMLNIVGGHE-ISOLATE 190 ????SqNYPIVQNaqqQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATpQdLNmMLWiVqGH CONSENSUS-A 194 CONSENSUS-B 185 CONSENSUS - C 191 CONSENSUS-D 188 CONSENSUS-F 174 CONSENSUS-G CONSENSUS-H 170 ....?-----7----V--AI------AV-----N--I----M-----??Y-I-T---AI---168 CONSENSUS-O CONSENSUS-CP2 ----??---???-?-??----??----?V---?-?-----?-?-?-?-?-?-?-?-?-?-?-?-?-? 107 DESIGNED SEQ QAAMOMLKETINEEAAEWDRVHPVHAGPIPPGOMREPRGSDIAGTTSTLQEQIGNMTN...NPPIPVGDI MUTATRD AAS QAAMOMLKETINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIGMMTN...NPPIPVGDI E-ISOLATE  ${\tt QAAMQMLKdtIneEAAewDr? HPVhAgPippgQmREPrGSDIAGtTStlqEqigwmTs... NPPiPVGdIagnameters and the property of th$ 256 CONSENSUS - A CONSENSUS-B 251 CONSENSUS-C CONSENSUS-D 255 CONSENSUS - F 239 CONSENSUS-G 233 CONSENSUS-H -G-L-V--EV----?--T--P??--L----I---T-----Q----?-T-R.??-??-----229 CONSENSUS-0 160

### FIGURE 3

MHR

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					Į	24 \/	V	<b>'p</b> :	2'	\/ p7			-motif /<-
DESIGNED SE				TACQGVG		rvlaea			ANI	MMQRGN			PN .
MUTATED AAs	TR	P	S		G		V	NN			R P	V	
ISOLATE-E	SILKA	LGTGA	TLBEMM.	racqgvg(	SPSHKA	RVLAEA	MSQA.	QH	<b>W</b> I	MMQRGNI	P. KGQTR	. IKCI	?N
CONSENSUS-A	sILr	Lg?g/	\tLe <b>EM</b>	macQgVg	gPgHK	ATVLABA	mSqv.	a??	?n??.:	i <b>M</b> mQrGn	f . rqqk	r?iKC	FN 38
CONSENSUS-B	TK-	Pa-					· <i>-</i>	tn-	s.at?		n-r	Ktv	~~ 39
CONSENSUS-C	T	P	·s		8		a.	nn .		8-	K-p-	-iv	38
CONSENSUS-D	tK-	P?-					a.	tn.	s-ta		K-pr	ki	39
CONSENSUS-F	TK-	P					a.	TN.	-?a	ks-	KR	-iv	38
CONSENSUS-G	T?-	P			?		A.	sg.	-A-A.?	?K??	K-P?	?	-? 361
CONSENSUS-H	??-		SI	~	?	•?	?	TN.	-?A?	}K	KR-	-I?	35:
CONSENSUS-0	OK;	p?-		V	T	.??	-A?AQ	ODFKG	GYTA.V	FQ	N.P?R-(	3	351
CONSENSUS-CP	Z :K-							r. ry. ·	-:v	B:-:-:	G? : ~ ? ~ ·		262
							cds ·						•
	Zn-mo	tif -	>/	/<-Zn-	-motif	->/	<b>p7</b> ⋅ \	<b>\</b>	'p1'	•	\/ p6		
DESIGNED SEQ	CGKEGH	LARNC	RAPRKK	GCWKCGKI	EGHQMK	DCTR	. RQANI	PLGKIN	PSNKG	. RPGNF1	PQSKP		
MUTATED AAs		ΙK		E	ž.				H	•	L R		
ISOLATE-E	CGKRGH	LARNC	RAPRKKO	SCWKCGKE	GHOMK	DCTR	ROANE	S Taktu		RPCNFF	OSKP.		
100												••••	
Consensus-A	CG)kEGI	ilarno	Craprio	:GCwKCgk	EGHQm	KdCT.?e	. rQAN	Flgki	wpSsK	G.RPGNF	pQsRp.		. 443
CONSENSUS-B													
CONSENSUS-C		·i		?					?		L?	?????	? 439
CONSENSUS-D		·1-K							b	<del></del> -	1	• • • • •	
CONSENSUS-F		1-K		r ?					n	· ·	Ŀ	• • • • •	- 445
CONSENSUS-G CONSENSUS-H		2				·		}	H		レーアーア。、	• • • • •	. 414
CONSENSUS-0				Q									
CONSENSUS-CPZ				RQ									
		vpr b	inding							v	or bind	ling	<b>p</b> 6
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			-			(minor			minor)	•	/<>	-	/ (80%)
DESIGNED SEQ MUTATED AAS	•	EPTAP	PAB	NF.	GFGEE7	T.PS	PKQI	EQXO.	KŒH	YPPSAS	LKSLFGN	DPLSC	)
ANA CLAILON				SI	R		Q	P	Ĩ	L		S	-
ISOLATE-E	• • • • • • •	eptap	PAE	NW.0	engee .	· · · · · ·		QKD	KBH	PPPSVSI	LKSLFGN	DPLSQ	,
CONSENSUS-A		. EPLA	PDAR	262	<b>^</b>								•
CONSENSUS-B	????	?	·-e	?f?	rf	16.81.,	pxq	egka.	.??ke	??pp1?s	lKSlFG	NDp1S	Q 485
CONSENSUS-C	??????	?	???	?????S	TF	r-rbacc	::q	-pı		1Y?a-	-r	g-	
CONSENSUS-D												x	479
CONSENSUS-F				5	-F?	<i>PS</i>	q			lya-			
CONSENSUS-G		:		7 .	フフフーニー	. 2 2 2		D22	-				482
Consensus - H				· · · · S- · ·	- P×	I- D-		- 22	•	•			440
Consensus-0		3			71	תכיצת	E-10.7 *		~ -	**	_		436
Consensus-CPZ			-I	Y.	??0?	K.?		G.,	: - <u>L</u>	FA-	1	-uş	444
				- <b>-</b> ·	•		: :			,,	?	??	- 333
CONSENSUS A-CP	Z FŔOM	LOS A	LAMOS I	HTV SEON	IPNOP		·n						

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-E SEQ FROM ISOLATE 93TH253 THAILAND

Underlined AA are not present in all overlapping segments

# FIGURE 3 (Cont)

### 5/216

Designed Se Mutated AAS	P B		ganssasrkl <i>g</i> dggg. R pt	D	
ISOLATE-E	PFRE.NLAFQQGKARBF	SSEQT0	ANSSASRKLGDGGG	AERQ	
CONSENSUS-A CONSENSUS-A ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CE	FPRE.NLAFQQGEAR?Fdpke-?????t	???????R	Rap-r-B-qVw-r- AP-tQV.RGSN RAPB-RVW-r- -PI-P-?GS RAPB-RVW-G-	nns-s???-EA-adrT.FSEAGAERQ .NP-SeT-A-R BGT-ES?G?? K.T-SET-A-R	3 4 4 3 4 1
	protease V	c- gag cds end			,
DESIGNED SEQ MUTATED AAS	GTSSSFSFPQITLWQRPLVTI	KIGGOLKEALLDIG	ADDTVLEDINLPGKWK EM R	PKMIGGIGGPIKVRQYD	
ISOLATE-E	GTSSSFSFPQITLWQRPLVTI				
CONSENSUS-A COMSENSUS-B ISOLATE-C CONSENSUS-D COMSENSUS-O COMSENSUS-U COMSENSUS-U	G???SF?FPQITLWQRPLVTVtVs	.k-gK  -GK  -K-GK  -VG-H-C-?  -RVGK		M	96 116 115 94 115 55
	OILIBICGKKAIGTVLVGPTPVNI	protease	\/ p66, p51		
ISOLATE-B	QILIEICGKKAIGTVLVGPTPVNI	igrnmltqigctin	PPISPIDTVPVKLKPG	MDGPKVKOWPLTEEKI -	
Consensus-à Consensus-b Isolate-c Consensus-d Consensus-o Consensus-u Consensus-cp2	QILIBICGKK?IGTVLVGPTPVN	L	AP	;	164 186 184 159 185 106
	M41L Kaltbickembeegkiskigpenp) A T K R	D67N	K70R		
SOLATE-E	Q Kalteickemeéegkiskigpenp)	ntpvpaikkostr	nrklydprelnkrtol	Pwevolgi Phpaglk	
Consensus-A Consensus-B CSOLATE-C	KALT?IC?EMEKEGKISKIGPENF			P	231 256
Consensus-d Consensus-o Consensus-u Consensus-cp2	BAQR BKDL	1?-	N	?PG P	254 227 255 164
WATED AAS	CKRSVTVLDVGDAYFSVPLDESFRK KD G	T		P PQ .	
SOLATE-E	KKSVTVLDVGDAYFSVPLDESFRK			•	
onsensus-a Onsensus-b Solate-c	KKKSVTVLDVGDAYFSVPLD??FR	i	i	A8	295 326
Onsensus-d Onsensus-o Onsensus-u	O?QED	I 	-1	ASD ASD AS	324 295 325
ONSENSUS-CPZ	?D		?		225

polymerase motif

## FIGURE 4

DESIGNED SEQ MUTATED AAS	QPIELPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIVPLTEEAELELEENREI  V E P R A E T A	· · ·
isolate-e	Q QPIBLPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIVPLTEEABLELEENREI	
CONSENSUS-A	QP??LPEKDSWTVND1QKLVGKLNWASQIYAGIK?KQLC?LLRGAKALTDIV?LTEEAELELAENREI	42
CONSENSUS - B	Iv	46
	IQTTTT	
ISOLATE-C	The state of the s	46
CONSENSUS - D	-sIkB	46
CONSENSUS-O	-?1Q?-?VBB	41
CONSENSUS-U	IQD-EPVK	46
CONSENSUS-CPZ	Z -?I????PI?-???-?-?-?	32
DESIGNED SEQ	.LREPVHGVYYDPSKDLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSAHTNDVRQLTEVVQKIATE	
NUTATED AAS	K I $\overline{I}$ G F F(error) A M G K AA $\underline{V}$	
ISOLATE-B	. LRIPVHGVYYDPSKOLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSAHTNDVRQLTEVVQKIATE	
:		
CONSENSUS-A	.LK?PVHGVYYDP?KDLVAE?QKQGQDQWTYQIYQEPFKNLKTGKYA?KRSAHTNDVKQLTEVVQKV??E	484
CONSENSUS-B	erm-GAiat-	533
	BFSIINF	
ISOLATE-C	B	531
CONSENSUS-D	B	
CONSENSUS-O	Q-DWV?I?-???EH?RQKASIRA?SQ-	479
CONSENSUS-U	BAIAQ-	532
CONSENSUS-CPZ		367
•	p51 \/	
	SIVINGKTPKPRLPIQRETWETNWMEYNQATNIPEWEFVNTPPLVKLNYQLEKDPIVGAETFYVDGAASR	
	K K A TD B AV N	
MUTATED AAS	K. K. A. TD	
	SIVIWGKTPKPRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVKLWYQLEKDPIVGABTFYVDGAASR	
ISOLATE-B		
CONSENSUS-A	SIVINGK?PKFRLPIQ?ETWE?WNMEYNQATWIPEWEFVNTPPLVKLWYQLEKDPI?GAETFYVDGAANR	550
	tkkt	602
CONSENSUS-B	BA-V	
ISOLATE-C -	R. A. ID	500
Consensus-d	E-I	600
CONSENSUS-O	?-?L?VTRTA?SI??E?	541
CONSENSUS-U	TEV	602
ONSENSUS-CPZ	????-?????????P????	416
	·	
ESIGNED SEQ E	tklgkagyvtdrgrqkvisltettnqktelhaihlalqdsgsevnivtdsqyalgiiqaqpdrsesevv	
TITATED AAS	IN D QQ L L K L	
SOLATE-E E	tklgkagyvtdrgrokvisltettnoktelhaihlalodsgsevnivtdsqyalgiioaqpdrsesevv	
	TO THE PROPERTY OF THE PROPERT	63.0
ONSENSUS-A	etk?gkagyvtdrgrqxvvsltettnqktelhaihlalqdsgsevnivtdsqyalgiiqaqpdrsese?v	618
ONSENSUS-B	1k1-	672
SOLATE-C -	I	
SOUNTE-C	L	670
ONSENSUS-D	?LEQ-K-?IIK-?AM-?L?KB???SSTQ-?-PI-	602
	farbana Edak - IIIka - Inana -	
onsensus-u	K	672
ONSENSUS-CPZ	????-?-??????-??QA?-?L????????-???L-	459
PETCHEN CEN S	QIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEHERYHSNNRTMASDFNL	
utated aas n	K K X	
	0	
SOLATE-E S	QIIEBLIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEHERYHSNNRTMASDFNL	
•	·	
onsensus-a	NQIIEKLI?K?KVYLSWVPAHKGIGGNEQVDKLVS?GIRKVLFLDGIDKAQE?HE?YH?NW?AMASDFNL	681
	sqK-EaeKs	742
	QS-ERBKSBK	
		740
ONSENSUS-D	sQK-EA	740
ONCENCIE-O (	QB-TK-E?TKIKDREQDKSL?-G-	669
ONCEMENTS IT	SEKSR	742
onsensus-u	????K?E?IS??-??	510
ONSENSUS-CPZ	77	J.,
	The state of the s	
ESIGNED SEQ P	PIVAKEIVANCDKCOLKGEAMHGOVDCSPGIWOLDCTHLEGKVILVAVHVASGYIEAEVIPAETGOETA	
DTATED AAS	P S I N I	
utated aas		

# FIGURE 4 (Cont)

	2	
ISOLATE-C	LRNBGIQB-	- 880
CONSENSUS-D		798
CONSENSUS-O	KK	882
CONSENSUS-U		631
CONSENSUS-CP	2b	631
DESTGNED SEO	AEHLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGP	
MUTATED AAS	R VS NL L	
MUINIED AND	<del>-</del>	
ISOLATE-E	AEHLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPINKGP	
Consensus-A	AEHLKTAVQMAVPIHNPKRKGGIGGYSAGERIIDIIA?DIQTKELQKQI?KIQNFRVYYRDSRDPIWKGP	880 952
CONSENSUS-B	T	952
isolate-c		950
Consensus-D	iiiii	950 865
Consensus-0		952
CONSENSUS-U		687
CONSENSUS-CP2		007
	vif cds ->	
DESTGNED SEO	AKILWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED	-
MUTATED AAS	A S	
ribinitus		
ISOLATE-E	AKLLNKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED	
•	·	929
CONSENSUS-A	AKLLHKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDC?AGRQDED	1002
CONSENSUS-B		1002
		1000
CONSENSUS-D	-QT-SMEQPGEIP	925
CONSENSUS-O	-QKIGKIGVGKIGTAN	100B
CONSENSUS-U	TO A DISCONDING	742
CONSENSUS-CPZ		/14

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-C FROM GENBANK U46016 HIV-1 SUBTYPE C (ETHIOPIA) ISOLATE-E FROM GENBANK U51189 HIV-1 SUBTYPE E ISOLATE 93TH253 (THAILAND)

### <- pol cds

DESIGNED SEC	MENTON O	WHITWH	TAMOUN	RTWNSI.VI	CHHMYIS	KKAKGW	PYRHH:	YESOHI	PKVSSE	VHIPLGE.	.ARLV	I .
MUTATED AAS	, MEMAN. 0	L	K	K	н	N	I	D R		D	1	
ISOLATE-E	MENRW.Q	.VMIVNQ	VDRMRI	RTWNSLVI	CHHMYIS	KKAKQWI	PYRHHY	/esqhi	Kasse	HIPLGE .	-ARLV	1
CONSENSUS-A	MENDN (	O WATUM	OVDRME	irtwinsly	кнімуу:	SKKARG	FYRHH	fesri	pkvsSE	VHI PLGd	ARL	VV 66
CONSENSUS-B				<b>k</b>		-0		Yt-	-rı			-1 66
ISOLATE-C	MONTON O	TOTAL TERMO	UDDMETI	TWINSTAKE	THMHTS	RRANGW	/YRHHY	DSRHE	KVSSEV	HIPLGE	ARLI	Ι.
CONSENSUS-D				K		?R-		Ya-p-	1	B		65
CONSENSUS-O CONSENSUS-CP	z -????.ī	<b>L-</b>	-?QKV	7KA	-Y-K-?-	-?-??N- ?-????-		Y????	???-	-155.	??? <b>K</b> -?	?- 34
	RTYNGLO	rcernen	เลยสมอ	PMBUKDA	STOVDPI	I.ADOLI	HLOYF	DCPSD	STIRRA	ILGQIVR	RRCBYF	<b>&gt;</b>
DESIGNED SEQ MUTATED AAS		R R		LS	010001	. н	H	A	A	HR S	Q	2
MOINIDO MAS			•	K		_	<u>¥</u>					
	RTYNGLQT	********	COMMICT	ENDONDA	e <del>ro</del> z dec	T.ADOT.T	нгоче	DCPSD	STIRRA	ILGOVVRI	RRCEYP	,
ISOLATE-E												
CONSENSUS-A	RTYWGLH	TGE : DW	ilghgvs	I EWrqKR	(STQvDP	DLADgL	IHLþYI	<b>FACES</b>	dsairk	AILGeiVF	FERCEA	Q 136
CONSENSUS-B	•		0	k			v	(	en	nE	3	- 136
ISOLATE-C	TO ISSUARY	YER DINK!	CHCVSI	<b>EWRLRSY</b>	NTOVDPG	LADHLI	нмнүг	OCLAE:	SATKKA	TPRIKADI	SKCDIQ	7
CONSENSUS-D	k		Q	KR		G	MY		87	2n	mv.	- 132 ? 118
CONSENSUS-0	TM	ID3B-		?Y-?-	KI	ETRM		-TT:		UK-T	122-2-1	K 76
CONSENSUS-CP2	Z T??-?-?			-?? <b>G</b> ?-	?	?T??	? ?	:		::::		K /0
•					VP:	r cds ·	->					
DESIGNED SEQ	SCHNICYGS	LOYLAL	KAL	ITPKKIRE	PLPSVK	KLTEDRI	NNKPQX	CIKGHI	RENHTM	igh		
MUTATED AAS	A		T	K K		R	B	T R	G			
ISOLATE-E	SCHINKVGS	LQYLAL.	KAL	<b>PTPKRIR</b> P	PLPSVK	KLTEDR)	MIKIPQX	CLKGHI	(EN P.I.M.	(CH2)		
CONSENSUS-A	AGHNKVG	SLOYLAL	.kAL	.VaPtkaK	PPLPSv)	KLtEDE	WnePQ	KTRGH	RG\$R?	₩gH\$		. 191
CONCENSING B			.a	.it-k-i-		?	. <b>–</b> – K – -	K	ht-			191
ISOLATE-C	<b>ACHNIKUGS</b>	LAYLAI.	TAI.	I KPKKAKP	PLPSVSI	CLVEDK	INKPOK	TRUKK	CHHIP	igh	•	
CONSENSUS-D	?		t	iK-I-	F	}	K	k	?HT-			186
CONSENSUS-O	260	T7	7-V	-K????-		)?	K??	?I-DQ	L?-?S-			161
CONSENSUS-CPZ	??Q:	???	?-?-???	??????R	?????	?	K??	R???-	?EN?TR			107

									-		
	*			<- V	if cds				•	LR domain	ı
/<-			olig	gomeriz	ation		->/			/<-	
DESIGNED SEC	MEO.	AP EDOGPO	REPYNE	WALELL	EELKOEAV	RHPPRPWL	HNLGOY	I YETYGI	TWSGVE	LIRTLOOL	,
MUTATED AAs		SS		T	н		Ğ	-	Ē	I	
.,01,		-		_	N		S	=	<del>-</del>	-	
ISOLATE-E	MEQ	AP EDQGPQ	REPYNE	MÄLELLI	SELKQRAVI	RHFPRPWL	HŅTGOA	IYBTYGD	TWSGVEA	LIRTLQQL	
CONSENSUS-A	ME?.	. AP . EDQGP(	QREP??	E??LELI	EETKHB3/	RHFPR?WI	LHGLGQ	HIY?TYG	DTWEGV?	AIIRILQQL	58
CONSENSUS-B	<b>q</b> ?:	??	yN	-Wt	?-A-	i	?	B	aB		65
ISOLATE-C	MEQ 2	AP EDQSSQI	REPYNE	WTLELLE	ELKNEAVE	CHFPRPWLI	<b>IGLGQY</b>	IYNNYGD	IWEGVEA	IIRILQQL	
CONSENSUS-D	Q.		YN	-Wt	S-A-	I	-s	?E	?B	-?	64
CONSENSUS-O	Q.	na	fN	-Wt	?-A-	p	-a	yB	m		66
CONSENSUS-U										S	67
CONSENSUS-CP	zQ	?-??		-WT-	?-N-A-	?P?-	????-	???-?-??	?????-	??????-??	33
	X.	R domain	->/ t	at cds	->					•	
DESIGNED SEQ	MFIH F	RIGCQHSRI	GIĽ		RNGASRS			•			
RUTATED AAS	LV	R	Ţ	G	S						
SOLATE-E	MPIH F	RIGCOHSRI	GIL	RQRRA I	RNGASRS					•	
ONSENSUS-A	LF?H.	FRIGCOHSR:	IGII	.?GRRG.	RNGA?RS	;					84
ONSENSUS-B	i-?	r	t	qa?	·s						· 93
SOLATE-C	LFVH P	RIGCOHSRI	GIF .	AREKROF	WSW						
ONSENSUS-D	I		t	.RQA.	SS- <i>-</i>						93
ONSENSUS-O		y								•	94
onsensus-u											96
ONSENSUS-CPZ	??I	????-??	L.	. PQR.	SSN						54
			-								

	intramolecular 3'sj 3'sj disulfide bonding \/ \/	:
	rev cds>/<- nls ->/	
DESIGNED SEQ	MDPVDPNLEPWNHPGSQPTTACSKCYCKKCCFHCQLCFLKKGLGISHGRKKR KORRGAPQSRKDHQYP	•
MUTATED AAS	K K T Y V T Y R R SE	
1	<u>О</u>	
ISOLATE-E	MELVDPNLEPWNHPGSQPTTACSKCYCKKCCWHCQLCFLKKGLGISHGRKKR KHRRGTPQSRKDHQYP	
CONSENSUS-A	M?PVDPnLEPWnHPGSqPtTaCskCYCK?CCwHCqlCFLnKGLGISYGrKKRr?RRgtPQs?kDhQnp	64
CONSENSUS-B	-erkktnkfvttQradSqtvs	68
CONSENSUS-C	?Ktk-sYlVqtqsa-?-SE	65
CONSENSUS-D	-d	66
CONSENSUS-F	-ELD	68
CONSENSUS-O	-DE?PH?-Q?P-NNRYYV??????AAAP-?KD-	55
CONSENSUS-U	-DKKKTKYPV	68
CONSENSUS-CP2	-D-?-????????-?-NNY??TK?-???T????\$?NN-D?	45
e	xon \/ exon	
DESIGNED SEQ	IPEQPLPQTRGGNPTDPKESKKEVASKTETDPCD	
MUTATED AAs	S SPD GE KEAP	
ISOLATĖ-E	IPEQPLPI1RGGNPTDPKESKKEVASKAETDPCD	
CONSENSUS-A	ipKQplPqtqg??ptgpkESkKkVeSKteTDrf?\$	95
CONSENSUS-B	Ls?s-pr-DrEP?d?	99
CONSENSUS-C	-sr-dBp-D-	98
CONSENSUS-D	SS-pR-d?Ap-Dw\$	99`
CONSENSUS-F	VIS-AR-N	96
CONSENSUS-0	V-?-S???-?RK.Q?RQB-QE??K??GP?G?P???SC??CTR?S?Q\$	83
CONSENSUS-U	SHRV.SEBD-	. 101
	22_22_2222	52

				bindi	-affinity ing site nls		
	\/ 3' sj	e	хоп \/ ехо		->/ <sup>:</sup>		
DESIGNED SEC	MAGREGETDE ELL	RAVRIINI	LYQSNPYPSSI	EG TROTRKNRR	LRRWRAROROIRA	ISERILSTCLA	GRS
MUTATED AAS	ם	K I K		SAR	B .HS	w nṗ	P
	N						
ISOLATE-E	magrsgstde ell	RAVRIINI	LYQSNPYPSSE	eggtrotr knrr	RRWRARQRQIRA	ISBRILSTCLO	ers .
CONSENSUS-A	MAGRSG?sDB.eLi						
CONSENSUS-B	d						
ISOLATE-C	MAGRSGDSDE ELL						
CONSENSUS-P	N-?T						
CONSENSUS-0		?QQ	?-?-	?N	RA-V-?	-A?-?-A-VV	HG? 56
CONSENSUS-U	DA						
CONSENSUS - CP	Z?E-??????-	??-VK	??-	??-?R-?·	???-???	????- <b>V-</b> ?-??	41
	Leu-ri	ch		•	•		
	effector	domain	•				
	/<-	->/					
DESIGNED SEO	AEPVPLQLPPLERLH	LDCSEDCGT	SGTQQSQGTET	rgvgrpoisges	SVILGPGTKN		
MUTATED AAs	N			N L	AV S	•	
				Š			
ISOLATE-E	TEPVPLQLPPLERLHI	LDCSEDCGT	SGTQQSQGTE1	GVGRPQISGES	SVILGPGTKN		
CONSENSUS-A	AEPVPLQLPPlerli	ıLDCsEdcg'	rsgTQq?qg?e	tGVGrpQvsVE	ssavLGSGTkn		. 120
CONSENSUS-B	t	?		?sil	-peE\$		115
ISOLATE-C	<b>AEPVPLQLPPLERLNI</b>	DCSEDSDT	SGTQQSQGTTE	GVGNP PREMA	TURE TRUNCATI	3D	
CONSENSUS-F	E??						105
CONSENSUS-0	Q?NN?VDQ-?					;	95
CONSENSUS-U	IC	G	PT-	S-PI-G	TIE\$		123
COMPONENCE _ CD7	DY_CD_P_P_DY_C	-0-V-TOO	W - CMTCADA	- NT- ETUDACCA	TVCTW_A	-	0.7

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									env e	cas ->	)   phos	2
									pho	- 1	i bios	•
DESIGNED SEQ	MTPL	EIIA	VAPIV	LIIAIVV	WTIAYI	EYRKL	LRQR	RIDRL	IKRTRERA	EDSGN	TES	
MUTATED AAs			L	L	VF	. <u>K</u>	K	K	EI			
CONSENSUS-A	mtPL???	elc)	IvGLiv	ALILAIV	WTIVg1	.eyKk	llkqr	Kidrl	?ikRIrER#	. EDSg	NES 5	57
CONSENSUS-B	-qs-	q-?-	a-v-	-a-i	£-	?r-:	i-R	?	d		5	6
ISOLATE-C	MVDLLAI	<b>VDÝRIV</b>	IVAFIV	<b>ALIIAIV</b>	MTIAYI	EYRK	LLRQR	RIDRL	IKRTRERA	EDSG	NES	
CONSENSUS - D	-Q							w-				7
CONSENSUS-F	-5??	LAIS	?TA	I	?Y-	R	-R	N	.YB??		5:	1
CONSENSUS-O	-H??	?LL-	?I??SA	L??INV??	-?F?	LR?	-?-??Q	DR?E?B-LER	.LR?-IR	.DD	Y 4	2
CONSENSUS - U	-Q- <i>-</i>	T-T-	v-	-F-A	-SY-	R-1	RK		.LD		51	7
CONSENSUS-CPZ	??	2353	?L????	???W?-CI	???I??	??-??Y	K???	??????-?	.??I?????	.?????	??- 14	4
DESIGNED SEQ	EGDTEE L	STM	VDM G	NYDLGVDN	INL							
TUTATED AAS	Ŕ	AL										
CONSENSUS-A	?GDT?E.	L?kL	VEM.C	nydlgvd	nNL\$						7	<b>'B</b>
CONSENSUS-B	eqe	-sa-??	???-	H?apwdv	dD						7	9
SOLATE-C . 1	DGDTEE L	STM	VDM G	<b>TLRLLDVN</b>	DL							
CONSENSUS - D	ErE	-sa	. <b></b>	HhAPwd?	Dcm-						8	-
	BAB										7:	
ONSENSUS-0	NSEE-OE										5	
ONSENSUS-U	DE	-ST	.M	<b>AEAI PDM</b>	D						8:	-
OMERNETIC - CD7	-20021	>_ > > > > > > > > > > > > > > > > > >	22222	PAND? ?	222DB						23	3

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### <- vpU cds signal peptide / gpl20

•	
DESIGNED SEQ MRVKETOMNNPNL WK W GTLILGLVIIC SA SD NLWVTVYYGVPVWRDADTTLFC	s
MUTATED AAS R M M M E E T	
CONSENSUS-A Mrvmgiq?nyq?l.wr????W.gtmilg??iIc.na??e.?lWVtVyYGVPVWkdaeTTLfc	
COMSENSUS-B ??k-rkrh-??????l-mlmse-te	
CONSENSUS-C:?x-w-gwiILGPwmlmvg.ne-k	
CONSENSUS-Dr?-erh????LmLMsv.a??E-t	
CONSENSUS-E Ket-m-wpnklv?sSd.Nrd	
CONSENSUS-F -?-R-M-R-W-HGKLLFiLne-Te	-
COMSENSUS-C -?-kr-W-HkLLVssn.nED	
CONSENSUS-O -t-tMKaM?KrNr.Kl?lylamALi-PLS??Q-YAsE?Pv	
CONSENSUS-U -?-?E7-R-??-????????-??-	
COMSENSUS-CPZ -??????-???-?.??-????????-???.?T??????	•7 19
•	
DESIGNED SEQ DAKAHETEVENVW ATHACVPTDPNPQETHLE NVTENPNMWKNNWVEQMQEDVISLWD QSLKPCVKLI	•
MUTATED AAS YD VV D D H I	
CONSENSUS-A dAkAydtE?HNVW?aTHaCVPTDPnPqBi?le.NVTB?FnmwkNnMVeQmheDiiSLWD.qSLkPCvkL	t 113
CONSENSUS-B	- 119
CONSENSUS-Ce?-V	- 119
CONSENSUS-Ds-k?-ai	- 117
CONSENSUS-EHev	- 121
CONSENSUS-FS-Ek-v	
CONSENSUS-Gs-s	
CONSENSUS-ONLTSqIsQ?-?-yp-?dIYd	
CONSENSUS-U?-??	
COMSENSUS-CPZ ?-???5?????-???V??????-??-??-??-??-??-??	
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DESIGNED SEO PLCVTINCTNANLINVN HYPERVARIABLE REGIONS 1/2	
MUTATED AAS	•
NUMBER AND	
CONSENSUS-A PLCVTL7C.???????????n?t????????????????????????	126
CONSENSUS-Bn_td????????????-???	
	133
CONSENSUS-Cn???	132
CONSENSUS-D	131
COMSENSUS-Entnal-nnv-ni-nvsniig-it?????	150
CONSENSUS-Pn-?t-at-?-?-q?tLkE	139
CONSENSUS-Gnt	143
CONSENSUS-O FQMntd1	129
CONSENSUS-Ut	105
CONSENSUS-CPZ -?-???P?????-??-????	60
^•^ ^^^	
•	
DESIGNED SEQ HYPERVARIABLE REGIONS 1/2	
MUTATED AAs	
CONSENSUS-A ??eikNCsfNmTtelrdkkqkvysLfYrlDvVqi????????????????????????????????????	. 160
CONSENSUS-B e??g-?????isive-akp-d?????	169
CONSENSUS-C -?a?Ai-pls	166
CONSENSUS-D -?q,mi?vkg-hak	165
	-
	185
CONSENSUS-F eP.gaQ	177
CONSENSUS-GemiiktE-Akp-n?sssd	182
CONSENSUS-On-??m-?-?VV-kE-KQAVs-L?k?N-tsT	164
CONSENSUS-U -??-?ii?kt?-akP-nn??	137
CONSENSUS-CPZ -??-????-???-???????-?????	73
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DESIGNED SEQ YRLINCHTSVIKQACPKVSFDPIPIHYCAPAGYAILKCNDKNFNGTGPCKNVSSVQCTHG IKPVVSTQL	
MUTATED AAS S A T IT E F N K T T R	
T	
$\mathbf{r}$	

### FIGURE 10

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CONSENSUS-	nrrkrk	234
	TO WE ARE THE TAXABLE TO THE TAXABLE	254
CONSENSUS-	3	
CONSENSUS-1	TWdYNk	245
CONSENSUS-C		251
		228
CONSENSUS-C	)	228
CONSENSUS-U	??-knKnK	- 205
CONSENSUS-C		120
CONSENSUS-C	E6	
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	<- V3 neutralization loop	_
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MUTATED AAS	VV PDV QKV S T	
HOINIDD /BID		
		220
CONSENSUS-A	LLnGSLAe???v?irSenitnNaktiiVql??pV?InCtRP.nnntr.ks???vri???gpGq??afya.	279
CONSENSUS-B	e.e.e-vf-dpes-e?ihrt.	296
CONSENSUS-C	eiil	291
	B.BiI	288
Consensus-D		-
CONSENSUS-E	e.eIiLh-NKs-estitvr.	312
CONSENSUS-P	e.diiqsdh-Nes-q	302
	e.eI?-dvnksie-?I?f	305
Consensus-G	and a second sec	
CONSENSUS-H	?D-T-NK???1???-?-	39
CONSENSUS-0	IT-Skg.kIr-Mgk?dsg-NT-N-?i-mt-eg-?-v.Qei?mW-S.	279
	E.E-i?dnet-k???	261
CONSENSUS-U		
CONSENSUS-CI	Z -??????-?????K?????V?????-E??-??G-?-?.???QMTN.	. 142
1/2 ne	eutralization loop -> CD4	
A2 116	eutralization loop -> CD4	
	•	
DESIGNED SEC	HYPERVARIABLE REGION 3/4/5	
MUTATED AAS	•	
MUINIED AND	·	
	22 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	222
Consensus-A	tgdiiG.dirqAhCnvsr?eWn?tlq?Va?qLr??f???nkt??iiF?n.ssGGD	320
CONSENSUS-B	?-???v-nq?	342
CONSENSUS-C	k?-ke-:?kK-aeh-pk?	334
	a company to the second company to the secon	221
CONSENSUS-D	-?r?????-?i-?a?kqk-qd?.lltkp	331
CONSENSUS-D	-?r???? . ? - ? i - ?a? k q k - gd? . l l t kp	331 360
CONSENSUS-D CONSENSUS-E	-?r???? . ? - ? i - ?a? k q k - gd? . l l t kp	
CONSENSUS - D CONSENSUS - E CONSENSUS - F	-?r???? . ?-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHnqP?p ?kqtqe?a?-ksh?k-ns	360 344
CONSENSUS-D CONSENSUS-E	-?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHn	360 344 344
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CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H	-?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHnk-ns?kgtqe?a?-ksh?	360 344 344
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CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O	-?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHn	360 344 344 65 321 306
CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O	-?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHnk-ns?kgtqe?a?-ksh?	360 344 344 65 321
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CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-U CONSENSUS-U CONSENSUS-C DESIGNED SEQ MUTATED AAS  CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-E CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-O CONSENSUS-O	-?r???? ?-?i-?a?-kqk-gd?.llkpk-y-EINgTk-e?-kqtek-ke. H- nn	360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336
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CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS  CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-G CONSENSUS-O	-?r???? ?-?i-7a?kqk-gd?.lltkp	360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 175
CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS  CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-G CONSENSUS-O CONSE	-?r???? ?-?i-7a?kqk-gd?.lltkp	360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 175
CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS  CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-G CONSENSUS-O	-?r???? ?-?i-?a?-kqk-gd? lltkp	360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 175

# FIGURE 10 (Cont)

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	9p120 / gp41	
DESIGNED SEQ	TPRPGGGDIKDNWRSELYKYKVVKIEPLGVAPTR AKRRVV EREKRA VG IGAMIFGPLGA I NMR E K I K Q L FL	
	?netFrPgGgdmrdNWrsELYkYKvVkiePlGvaPtr.akrRVVeREKRA??vg.lGavflgflGa	
Consensus-A	-t-i	
CONSENSUS-B	-???:?:	
CONSENSUS-C	-?	
CONSENSUS-D		
CONSENSUS - B	NiKQi,IMif	
CONSENSUS-F	-?n-k?l?l	
CONSENSUS-G	kk	
CONSENSUS-H	21/	
	?-1?k-ITfrvK-FSki-RP?Igt?t?HMLv-S-	
CONSENSUS-O	-?	
CONSENSUS-U CONSENSUS-CPZ		
DESIGNED SEO	agstmgaasitltvoarollsgivooosnllraikaoohlloltvmgikoloarvlaverylkd okplo	
MUTATED AAS	M T N W I OT	
CONSENSUS-A	AGSTmGAaSiTLTvQarqLlSGIVqqQsNllrAleaQqhlLkLTVNGIKQLQARvLAvErYLrD.QQLLG	
CONSENSUS-B		
CONSENSUS-C	tik	
CONSENSUS-D		
CONSENSUS-E		
CONSENSUS-F	0	
	???????	
CONSENSUS-G		:
Consensus-H	ATatht-?KQ?R-SR-LL-TliQNn	
CONSENSUS-0		
CONSENSUS-D		
CONSENSUS-CPZ	????????????	•
	* * ^^^	
CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - G	INGCSGK1ICtTnVPWNSSW	5 5 6 6 5 5 3
	\/ 3'sj	
DESIGNED SEQ DI MUTATED AAS	RNEQELLELDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSFQTLLPA  KD A N SK V I I T	
	EKNEQdLLaLDkWanLwnWPdIsnWLWYIriPimIVGGLIGLRIvfaVlsiInRVRqGYSPlSFQtltp?	6
	EKNEGOLLALUKWANDWNWFOISHWUMIIIIFIWIYOGDIOANYYLUVAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	6
	ee	6
onsensus-C	kg-??-t?ki	6
ONSENSUS-D	e?Ss-T?k	
MODNOTIC P 1	npveSTK1VP:nn	7
MATHERIC P		6
	. 20 с 2 2 2 2 2 2 2 2 2	6
MODING!!C. O		6
**************	C Y PCCG_TYT_FT_FT_F	6
Onsensus-U - Onsensus-CPZ -		3
4	<- tat cds	
DESIGNED SEQ PI OUTATED AAS	RG PDRPEGIEEEGG EQDRDRSVRLVSGFLALAWDDLRSLCLPSYHRLRDLILI A AR IVELLGHS LGR RG G N S N F V T R	

## FIGURE 10 (Cont)

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CONSENSUS - O CONSENSUS - U CONSENSUS - CP.	q?E.agT-0 G6	5-T	-E-NN	·V	N		E	I		L	.v	N	G-R	685
CONSTRUCTOR	<b>.</b>				• • • •		rev cd	·	<b>6</b> 3-13	LINCH		_ # # WIL	71P	. 398
DESIGNED SEO	SLRGLRRG	WEAI	KYL W	ILLOY	WGOE	LKTS	avslina	TATAV	AEGT	DRVT	EVAO	RAGRA	TT.HT	
MUTATED AAS	K Q	G	WG	Ĺ	L	N			GN	I	v	W	N	
CONSENSUS - A	slkglrlg.	weg	lkYL.	NLlly	MgrE	LK?	AinLld	tiAia	vAqvt	:DRv1	Eige	riak	Ailnı	780
CONSENSUS-B	?:??	a	w	g-	sq-	n-	-vsn	at	Eg-		-vv-	-a?-	h-	789
CONSENSUS - C	rqr	a	~G	s-vq-	·ī-	k-	s		EG-	i-	~??~	?	?	787
CONSENSUS - D	R													773
CONSENSUS-B	R													832
CONSENSUS-F	.?RR													787
CONSENSUS-G	i				a-	N-	~?		N		-vv-	-aC		800
Consensus-o	lI?y-gU	WIlGQktle	CR-C7	4v?Q-	-LQ-	-qn-	- <b>T</b> -	?-V-	-N	-qi-	lGi-	?G	;	767
CONSENSUS-U	R	A	G	V	0	N-	SNA	TV-	-EG-	I-	-v	C		741
CONSENSUS-CPZ	I-HSL	R~R	-CL GC	311Q-	K-	I~	sA	T	- EG-	I-	-AF-	VTL-I	-R	460
DESIGNED SEO	PRRI ROGLERA	ALL.		•								-		
MUTATED AAS	T P						·							
CONSENSUS - A	PrRIROGIE	aLl\$												793
CONSENSUS-B	-?													801
CONSENSUS - C	F-a	q-												800
CONSENSUS-D	-?													785
CONSENSUS - E			•										•	. 845
CONSENSUS - F	-??													798
CONSENSUS-G														813
CONSENSUS-0		?											•	779
CONSENSUS - U	P													754
Consensus - CPZ										_				473

DESTGNED SE	Q MGGKNSKSSLVGNPEVRERIR	QT	PPAAEGVGAVS	DD LDKHG	aitssntp.	A
MUTATED AAS		RA	A A	R <u>Y</u>	L A	
7,033.03						•
ISOLATE-E	McGknskssivgnpqvrbrik(	QT TQ	PPAAEGVGAVS(	DO LDKHG	avtssnm	
	•	_			d marma n	
CONSENSUS-A	MGGKWSKsSiVgWPeVrkRmRc	<b>3T</b> ?	PEAALGVGAVS	rokue	LIPSSNE?:	2 41
CONSENSUS-B	?-?-??e1		PDG1	n Inve	ALTSSNTP)	
ISOLATE-C	MGGTMSKCSPVGNPAIRERIRE		APAAEGVGAASE			
CONSENSUS-D	AI-E-I-x	C-??????	app	(b	2u-bv	3 3 3 6
CONSENSUS-O	NA??-?KF????F	(?	. bC-b::-	22222_2_2_2		. 31
Consensus-U	????????-E-I-?	·	- <b>P</b> ::::-		A-	
\vskip6pt	* SH3-binding	SH3-I	binding			
	•					•
DESIGNED SEC	NNADCVWLK AQE E EG V	GFPVRPQVPLRPMTYK				•
MUTATED AAs	PAE E	1	A V L	DIQ	D	
					0071 DI (#1	
isolate-b	NNADCVWLR AQE E EG V	GPPVRPQVPLRPMTYK(	Sapdlspflkek	GGTEGTAARKK	ORITOFMA	
	tnpsCaWLE?Aqe?.de?.V	COMMON NAME TO THE PROPERTY.	. APOT C'A ETT MORT	eer.ner.russkip	ORTIJIJAV	110
CONSENSUS-A	ade??-e?	GE LAK LUAL TENT	-2		-d	108
CONSENSUS-B	NNPDCAWLE AGEE B BE V	CEDUDOUDI DEMTVK	APDISIPIKEK	CLEGITYSKKR	DETLIDLING	200
ISOLATE-C	adESE	GPPVRPQVPLRPM11R	or desperance	BW-K		115
CONSENSUS-D	N-AAL-P-7.SH??		- P P	?H	A	93
CONSENSUS-O	N-??-???E?E		-F?	??		83
Consensus-U	N-55-555-155-1E51-E.		• ,•			
\wskip6pt	•					
(VBKIPOPE		SH3-bindin	9			•
	-	*			•	•
	·			M T HOMOOHOMEI	DEPRESENT T	
DESIGNED SEQ	YHTQGFFPDWHNYTPGPGIRY F			ianonyemanaa. LDI	D K	
MUTATED AAS	и у о т	S	AB	ш	D . K	
	Y YHTOGFFPDWHNYTPGPGIRY P	A COORDINATE AND DOOR	UP POWERENCE	T.T.HDMSCHGTRT	REPRVI.T	
ISOLATE-E	YHTUGFYPDWHNITPGPGIKI P	PCLGMCLITTALADAKE	AP PDWWREIGHT		22,020	
	YnTOGEFPDWONYTPGPGERE.P	T.TECSACERT.VDv/DDaE3	VR eat?GENNS	LLHPI COHGodD	e?revLm	176
CONSENSUS-A CONSENSUS-B	-hy	e-ek	ne	msl	pB?	174
ISOLATE-C	YNTOGFFPDWONYTPGPGVRY P	T.TFGWCFKT.VPVDPSE	VE RINEGENNO	LLHPASLHGMED	EDREVLK	
CONSENSUS-D	II-Y		Et-c	?B-	pB-qk	182
CONSENSUS-0	-?	S?R-1	A-RIGNT?-?A?	A-??B-	?H?~X~?	150
CONSENSUS-U	-H??-?-?-?-	-???-?-	иC	?5?-	?E?	138
LONSENSUS-U		•				
vskip6pt	•					
,	,	<b>.</b>				
		•			_	
ESIGNED SEQ	WKFDSRLARRHIARELRPEFY KI	DC			-	
nutated aas	H L M H Y					•
SOLATE-E	WKFDSALARRHIARELRPEFY KI	DC				
	www.columbar alkiwaaniumpar w	nce.		•		199
ONSENSUS-A	wkfDsrlalkhra?elhpefy.KI	つすでMCT_CCででDDなたすぐ つすでMCT_CCででDDなたすぐ	DENDI CCTCELL	RAT.RCCT		230
	-rth-m-ry		WPWTOO I GDUI		_	
	WKFDSHLARRHMARELHPEYY KI				•	206
ONSENSUS-D	-R-NfB-K-R-m				· · .	166
ONSENSUS-O	-?RS-G?T-???LF?-?				-	157
MARCHICITO II						131

# FIGURE 11

GAG OVERLAPPING SEGMENTS

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# FIGURE 1.

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171	ングエム
	4

Segment 12	Segment 13	Segment 14	Segment 15	Segment 16	Segment 17
PEVIPMFSALSEGATPQDLNMMLNIVGGHQHQ T cet gag gte atc cet atg tte wea gec etc age gaa gge get ace eec caa gae etg aat ayg atg etc aac aye gte gge gga cac caa	PODLNMMLNIVGGHOAAMOMLKETINEEAAA T cct cag gat ctc aac ayg atg ctg aat ayt gtg gga ggc cat cag gcc gct atg caa atg ctg aaa gas aca atc aat gag gaa gcc gct	AAMOMLKETINEEAAEWDRVHPVHAGPIPPVA	EWDRVHPVHAGPIPPGOMREPRGSDIAGTT I 988 tgg gat agg rtt cac oct gtg cac gct ggc cet rtc sct ccc ggc caa ats aga gag cct agg gga agc gat atc gct ggc aca acc	GOMREPRGSDIAGTTSTLOEQIGWMTNNPP I gga cag atragg gaa ccc aga ggc tcc gac att gcc gga acc aca agc aca ctg caa gag caa atc gga tgg atg aca arc aat ccc cct	STLOEQEOIGWMTNNPPIPVGDIYKRWIILGL A S V E E toc acc ctc cag gaa cag att gsc tgg atg aca art asc cct ccc rtc cct gtc gga gas att tac ata agg tgg att atc ctc ggc ctg

21	121	
ΖI	/ZI	O

	Segment 19	Segment 20	Segment 21	Segment 22	Segment 23
IPVGDIYKRWIILGLNKIVRMYQPVSILDI	NKIVRMYQPVSILDIRQGPKEPFRDYVDRF	ROGPKEPFRDYVDRFYKTLRAEQATOG BVKN	YKTLRAEQATOBVKNWMTETLUVONANPDC	WMTETLLVONANPDCKSILKALGTGATLEEED D T R P C C C E E T S S S S S S S S S S S S S S S S S	KSILKALGTGATLEEMMTACOGVGGPSHKA
V	S	K	F		T R P S
rtt ccc gtg ggc gaw atc tat aag aga tgg atc att ctg gga ctc aac aaa atc gtg aga atg tat yma ccc gtc agc att ctg gat atc	aat aag att gtc agg atg tac yma cct ctc tcc atc ctc gac att arg caa ggc cct aag gaa ccc ttt agg gat tac gtc gac aga ttc	ara cag gga ccc aaa gag cct ttc aga gac tat gtg gat agg ttt twc aaa acc ctc agg gct gag caa gcc wca cag gaw gtg aaa aac	twt asg aca otg aga gcc gaa cag gct wcc caa gas gtc aag aat 199 atg acc gas aca ctg ctc gtg caa aac gct aac cct gac tgt		ass was att ctg axs goc ctc ggc mas ggc gct we ctc gag gaa atg atg aca gcc tgt cag gga gtg gga ggc cct rgc cat aag gct

M M T A C Q G W G G W G G P S H K A R W L A B A M S Q A T H A N I M A M S Q R W R W N N N N N N N N N N N N N N N N

						•	3372
Segment 30		Segment 31		Segment 32		Segment 33	
PTAPPAENFGFG S R S	tc ggc	SPKOEOKDKE	. අයු යුසය	E H Y P P S A S L K S L F G N D	aat gac		
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Ī <b>u</b>	S D	×	8 8	Íτι	tg t		
z a	cco cct goc gaa are ttt rga ttc	O F	tto gga gag gaa acc aca cco tco cma aag caa gag cma aag gat aag	H	aag tee etg ttt gge		
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<b>A</b>	ř Ř	Q	Ď	×	t B		
ф	g g	¥	<b>8</b>	귀	ago oto		
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<b>A</b>	gag oot acc got	വ	Ö Ç	K	tya gcc		
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다 편	arg cct	闰	eğ D) D)	≯	aaa gaa cwc tac ccc cct	Ы	ດ ຕູດ
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O)	280	[z.	tte	X	88	Z	88
다고	cyg	ល្	tto rgg	Д	aaa gac	Q	99
Į:	tto	ĮΞŧ	tt	×	888	[II.	t .
и г г г г г г г г г г г г г г г г г г г	ggc aat tto cyg	Z U	gag art	A D X	gaa cmg	SITONDAIS	Second the ggs ase gat eee tys tee eas
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<u>ы</u>	act	臼	gaa	- [→	8 2 8	Д	cct ccc
_ '≥	tgg (	Д	8	<u> </u>	gag	<b>&gt;</b> 4	tat
Н	att	M P		<b>E</b>	889	(H)+	**

POL OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
FRENLAFQQGKAREFSSEQTGA   P C C C C C C C C C C C C C C C C C C	SASRKLGDGGGA] PT Cyct rea age aga ctg gga gae gga gge gga gee	c 99c 9at 99c 99a 99c 9ct 9aw a99 caa 99c acc tcc ago	c cet cag att acc etc t99	ang att gga ggc caa ctg awa gaa gcc ctc ctg gat aca	t aca gtg ctc gag gas

Segment 14 Segment, 15 Segment 16 Segment 17 aag ctc gtg gat ttc aga gat tto tgg gag gto cag oto ggo aca gtg aaa agc gtc acc gtc ctg gat gtg gga gac gct tac ttt agc gtc ccc ctc gac raa rrc Н R S D S  $\mathcal{O}$ gcc A, 田瓦 ſτι gtg O ſτι A > Д अनुव टर्ड क्षक क्षत्र क्षक क्षत्र रटट ഗ П Дı Ы 团 ¥ Д H × ⋈ ¥ > tat aac toc acc aaa tgg aga Z ፎ Ē, × Ŋ ĸ Д ſτι gag ctc aac aaa agg aca cag Д ¥ O Н × Z H Н Ç ď gag cac cct got 团 Ŋ 召 ď Ω cct gac Д × Д Д Ö 330 ಡಿಕೆದ ಡಿಡಿಲ್ಲಿ ಡಿಡಿಡಿ ಡಿಡಿಲ್ಲ Ö × z > 工 att act  $\mapsto$ ¥ Ы Дí Ω tcc arg gga atc K 民 × 闰 Н Ы 899 ഗ Н 召 Ö > gct gac ttt ctg asa atc Н ď ſъ Н ⊱ Caa × بحرا Q Д > 286 gtc gtg Ö > > Ŋ ctg gaa gaa tac aat acc cct 团 Д Ы 闰 노 団瓦の。 888 gac ttt tgg बबब बबद्र Н 노 × ⋧ gaa 闰 z ĸ × ц atg **tgg** ctc aag Σ × Z Д ¥ gct gaa aag Caa 闰 Д ¥ O Ы Bac aca 990 acc  $\bowtie$   $\vdash$ Z H Ö Η gaa tgt gat agc aga U 团 Ø 召 ď atc S ρι Д ĸ ρ, **BEE5** gga 田人 ¥ Z 工 acc ctg att ccc Н ¥ Ы Д ctc X R g Ы ĸ 团 Н

Segment 18		Segment 19		Segment 20	c	Segment 21	Section 20	77 mamaa
L D V G D A Y F S V P L D E S F R K Y T A F T I P S I N N E K D	Cto gae gto gge gat gee tat tte tee gtg eet etg gat raa rre tte aga aag tat ace get tte aca ate eet aer ava and	ttt agg aan tac aca gcc ttt acc att ccc tcc ayc aat aac gaa acc cct ggc att agg tat cag tat aac gtc ctc cr ca can acc	T P G I R Y Q Y N V L P Q G W K G S P A I F Q S S M T K T T	P Q C CC atq mcc mas at	KGSPAIFQSSMTKILEPFRIKNPEMVIYOV	K Q $oldsymbol{D}$ Late tit cag tee age atg mea mag att etg gag eet tit agg awa maa aac eet gas atg off and $oldsymbol{D}$	EPFRIKNPEMVIYQYMDDLYVGSDLEIGOH	mag aat ccc gaw atg gtg att tac caa tac atg gac gat ctg tat gtg gga agc gat ctg gaa atc gga ca
						-	_	JI

Segment 23		Segment 24		Segment 25		Segment 26	•	Segment 27	
DDLYVGSDLEIGQHRTKIEELRAHLLRWG A	Q g gat gac ete tae gte gge tee gae ete gag att gge caa eae agg ree aaa ate gaa gag ete agg 8ma eae ete etg axa tgg gga	TKIEELRAHLLRWGFTTPDKKHQKEPPFL A	rca aag att gag gaa ctg aga	ттроккнокерргимсуецнрокитиор se	t acc aca ccc gat aag aaa cac caa aag gaa ccc cct ttc ctc tgg atg gga tac gaa ctg cat ccc gat agg tgg acc gtc cag cct	MGYELHPDRWTVQPIELPEKDSWTVNDIQ V	Q g atg ggc tat gag ctc cac cat gac aga tgg aca gtg caa ccc atc awg ctc ccc gaa aag gas tcc tgg aca gtg aat gac att cag	ELPEKDSWTVNDIQKLVGKLNWASQIYAG Seg V	Q BWg ctg cct gag aaa gaw agc tgg acc gtc aac gat atc caa aag ctc gtg gga aag ctc aac tgg gcc tcc cag att tac
Σ	atg	×	<b>8</b> 55 8	Íτι	t t	Z	£99	н	a t t

Segment 28	Segment 29	Segment 30	Segment 31	Segment 32	Segment 33
LNWASQIYAGIKVKQLCKLLRGTKA PR ctg aat t99 gct agc caa atc tat sct 99c atc aaa 9t9 ar9 caa ctg t9t aa9 ctc ctg aga 99c rcc aaa 9cc	LCKLLRGTKALTDIVPLTEEAELELEL A E T ctc tgc aaa ctg ctc agg gga rca aag gct ctg aca gas att gtg mca ctg aca gag gaa gcc gaa ctg gaa ctg	PLTEEAELELEENREILREPVHGVY T mca ctc acc gaa gag gct gag ctc gmg gaa aac aga gag att ctg arg gaa ccc gtc cac gga gtg tat	ILREPVHGVYYDPSKDLVAEVQKQG III atc ctc ara gag cct gtg cat ggc gtc tac tac gat ccc tcc aag gat ctg rtc gct gaa rtc caa aag caa ggc	DLVAE(V)QKQGQDQWTYQIYQEPFKN I G F F gac ctc rtt gcc gag rtt cag aga cag grt cag tgg aca twt cag att twc caa gag cct ttc aaa aac	YOIYQEPFKNLKTGKYSRKRSAHTN F A M G twc caa atc twt cag gaa ccc ttt aag aat ctg aaa acc gga aag tat kcc aga awg aga ryc gct cac aca aac
X 88 88 88 88 88 88 88 88 88 88 88 88 88	O1 80	9 ودم	田 点	보 <sup>8</sup> 8	[H $^{8}_{\Omega}$
ည စိ	X X #	H g	저 8 gg a	ည နို့	Q W caa tgg
	V V	<b>Сы</b> §	Z ag Z	р 8 8	Q g
L. V	<b>⋈</b> 8	[- 8	田 ga g	D g	O O g
<b>⋈</b>	a H	크 닭	E A B	tat	O g

GIGURE 12 (Cont)

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Segment 40	Segment 41	Segment 42	Segment 43	Segment 44	Segment 45
SRETKLGKAGYVTDRGRQKVIS N art agg gaa acc aaa ctg gga aag gct ggc tat gtg aca gac aga ggc aga cag aaa rtc rtt agc	GROKVISLTETTNOKTELHAIH IV D 998 agg caa aag rtt rtc tcc ctg aca gas acc aat cag aaa acc gaa ctg caw gcc att cam	TELHAIHLALQDSGSEVNIVTD QQQ aca gag ctc cam gct atc caw ctg gct ctg caa gac tcc ggc tya gag gtc aac att gtg aca gac	EVNIVTDSOYALGIIQAQPDRS L K gaa gtg aat atc gtc acc gat agc caa tac gct ctg gga atc att cwg gct cag cct gac ara agc	QAQPDRSESEVVSQIIEELIKK L Cwa gcc caa ccc gat arg tcc gag tcc gtg art cag att atc gaa vag ctc atc aaa aag	EELIKKEKVYLSWVPAHKGIG KSRAA
U	<b>5</b> 7	מ	ţn.	Ŋ	a t t
	지 <sup>899</sup>	A ag		a to	B tt
A	gat	O, ga	D gg	att H	O, g
ggc	E Soci	a a B	လ နဲ့ရ	D gg	V S N gtg art
D	p gtc	H 808	g g	t t	9 tg
gtg	۲ tac	EH SS	Ox g	₫ obe	gt C ←
tat tat	ධ <sub>අහු</sub>	E C E	g F	≯ tg	回 ga g
FT FJ	A gec	E S	d oob	O gan	က ဦ
aca T	X 8 8	H g	H g	ស ភ្ជុំ	[년 50 50

FIGURE 12 (Cont)

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Segment 51	Segment 52		Segment 53		Segment 54		Segment 55		Segment 56	
Q L K G E A M H G Q V D C S P G I W Q L D C T H L E G K V I I N I caa ctg aaa ggc gaa gcc ats cat ggc caa gtg rat tgc tcc ccc ggc att tgg caa ctg gat tgc aca cac ctc gag gga aag rtt atc	GIWQLDCTHLEGKVILVAVHVASGYIEAEV T	L gga atc 19g cag ctc gac 1gt acc cat ctg gaa ggc aaa rtc att ctg gtc gcc gtc cac gtc gcc tcc ggc tac att gag gct gag gtc	LVAVHVASGYIEAEVIPAETGQETAYFLLK	1. ctc gtg gct gtg cat gtg gct agc gga tat atc gaa gcc gaa gtg atc cct gcc gaa acc gga cag gaa acc gct tac ttt mtc ctc aag		L K T' att ccc gct gag aca ggc caa gag aca gcc tat ttc mtt ctg aaa ctg gct ggc aga tgg cct gtg ara ryc att cac aca gac aat ggc	VIHTDNGSNFTSA	K. 1. Ctc gcc gga agg tgg ccc gtc arg rya atc cat acc gat aac gga agc aat ttc aca agc rct rcc gtc aag gct gcc tgg tgg gct	AVKAACWWA	. G t gtg aaa gcc gct tgt tgg tgg gcc rz

Segment 57		Segment 58		Segment 59		Segment 60		Segment 61		Segment 62	
QEFGIPYNPQSQGVVESMNKELKKIIG Segment 5	caa gag ttt ggc att ccc tat aac cct cag tcc cag ggc gtc gtg gaa agc atg aac aaa gag ctc aag aaa atc att ggc	QAEHLKTAVQM	$oldsymbol{D}$ gag toc atg aat aag gat at atc gga cag gtc agg gam cag got gag cat ctg aaa acc got gtg caa atg	QAEHLKTAVQMAVFIHNFKRKGGIGG	ugas caa gco gaa cac cto aag aca gco gto cag atg gco gto tto att cac aat tto aaa agg ara ggo gga ato gga ggo	IHNFKRKGGIGGYSAGERIIDIIATDI Segment	ı 99c att 99c 99a tac tcc 9cc 99a 9a	DIQTKELQKOITKIONF	$\sim V$ . $\sim$ Sgc gaa agg att xtc gat atc acc act cag tat ang gaa ctg caa aan caa atc mya ang att cag aat ttc	KIQNFRVYYRDSRDPIWKGP	$\Gamma$ $\Gamma$ Gag ctc cag aam cag att myc aaa atc caa aac ttt agg gtc tac tat agg gat agc aga gac cct mtc tgg aag gga ccc
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Segment 63		Segment 64	Segment 65		Segment 66	
KVIIKDSKUPIWKGFAKLLWKGEGAVVIQD Segment63	Loc agg gat ccc mtt tgg aaa ggc cct gcc aaa ctg ctc tgg aaa ggc gaa ggc gct gtg gtc atc caa gac	KGEGAVVIQDNSDIKVVPRRKAKII Segme	KVVPRRKAKIIRDYGKQMAGDDCVAG Segme	gtc ccc aga agg aaa gcc aaa atc att agg gat tac gga aag caa atg gct ggc	DCVAGRQDED	$A$ $egin{array}{cccccccccccccccccccccccccccccccccccc$
۲. ۱	aga gac	W K tgg a	<u>ب</u>	aaa gtg	یج	18g C
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VIF OVERLAPPING SEGMENTS

## 36/216

Segment 4

VIMVQW	tgg caa gtg	TWNSLVKHHMYISKKAKGWFYRHHYE K	tac tgg	AKGWFYRHHYESQHPKVSSEVHIPLG N	gct aas	KVSSEVHIPLGEARLVIRTYWGLQTG D I K H	aaa gtg to
Z H	itg at	r v	las aci	<b>S</b>	iga tg	ω Ω	cc ag
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E A R L V I R T Y W G L Q T G E (K) D W Q L G H G V S I E W R D I K H Q Q R C aga ctg rtt atc ara acc tat t99 99a ctg caw acc 99a aga ctg caw gc egg cas ctc 99c caw 99c gtc agc att gag t99 agg

⊚∺

Segment 10 gga cac aat aag gtc ggc tcc ctg caa tac ctc gcc ctc gtg agm agg aga tgc gaa tac cct aag aaa atc ara ccc cct ctg cct agc gat cas ago rea ate OŒ ß Н ď А HK 闰 Д 900 Ы Ø O Н ß tgc ttt kcc gat ags tat age aca cag gte gae cet gre ete × Д ы Ω 召 O Д ĸ D U SA Ы 民民 **足** 0 Д ſΞŧ ល А U > н gat gga cas aka > Ω нα Ü K ĸ > OH O) Ľτι × Qι Н Ö aga gcc att ctg ctc yas  $\bigcirc$ H $\triangleright$ z H K ഗ Н gtg gga age ete cag tat etg get etg amg get etg att Ы H н × н CAC ט ď, Ц **克** 50 耳 N 4 × 888 Ø 民 ĸ Н Y P Q Lat cmg att agg gac caw ctg ада шмд X H Q T K ы 異 OH Д ፈ Н tgg rcc gag K HK 闰 Ω 3 agg tgt atc gaa ы U ď, ល 闰 gac ctg ы R × Н А ton grt tte ket æ Ø D D SA ß gtg ス S gg Ы Д > Ŀ tgt gtc **9**9a > Ω ഗ U O CAB H ᅜᅥᇏ 氏 の 注 > Ω Ü 99a tt OH 3 Caa O Į, > U × X Ы Н Ü Caw tac Хак got ato oto スHV Ц Z OH ß tgg tac 耳 × Ы Н Z gat cat Ö വ വ 耳 Ø Д 0 A X K × н വ് P O E ĸ O T X Ы 闰

FIGURE 12 (Cont)

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Segment 11		Segment 12
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VPR OVERLAPPING SEGMENTS

## 39/216

Segment 1		Segment 2		Segment 3		Segment 4	
E 1 K 0 E A 1 E A	$\Gamma_{ m N}$ tgg rcc ctc gag ctc ctg gaa gag ctc aag mam gag gct	PWLHMLGQK	gag gaa ctg aaa maw gaa gcc gtg aga cac ttt ccc aga ccc tgg ctg cat rrc ctc ggc caa yac	SGVEAL	Since of the seasing the season of the seaso	ALIRTLQQLMFIHFRIG I L V	tgg kma ggc gtc gag gct ctg atc aga avc ctc cag caa ctg mtg ttt rtc cat ttc aga atc gga
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闭	t gag		a B	<b>≯</b>	c ta	먾	<u>ت</u> ت
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FIGURE 12 (Cont)

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Segment 5		Segment 6	
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J	agg ayc ctg caa cag ctc mtg	ഗ	agc
EН	ayc	Ħ	cat
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н	att	ט	tgt cra cat agc aga atc gga atc myc

TAT OVERLAPPING SEGMENTS

## 41/216

Segment 1		Segment 2		Segment 3		Segment 4		Segment 5	· .
КСУСККС	atg gaw cyc gtc gac oct aas otc gag oct tgg aaw cac oct ggo too cag oct amg aca goo tgt wmo aaa tgo tat tgo aaa aag tgo	KCYCKKCCFHCQLCFLKKGLGI Y V T	m N agc caa occ ama acc got tgc wmc aag tgt tac tgt aag aaa tgt tgc two cac tgt cag sto tgc ttc otg ama aag gga otg gga atc	GRKKRKQRRGAPQ	V t cat tgc caa stg tgt ttt ctc	О В В В В В В В В В В В В В В В В В В В	I S S S S S S S S S S S S S S S S S S S	©рночегрегроткасирторкезкк	G E t ccc aca grc cct rag gaa agc aaa aag
	-		_	_	-		_	-•	-

Segment 6

FIGURE 12 (Cont)

QTRGGNPTDPKESKKEVASKTETDPCD PDGE EKEVASKTETDPCD caa mcc aga ggc grt aac cct acc grt ccc raa gag tcc aag aaa rag gtc gmg tcc aag rca gag aca gac cct tkt gac

different

REV OVERLAPPING SEGMENTS

## 43/216

Segment 1		Segment 2	Segment 3	Segment 4	Segment 5
MAGRSGSTDEELLRAVRIINILYQSNPYPS D N	atg got ggo aga ago gga rro aca gao gaa gag oto otg arg got rto aga ato att aas att otg tat cag too aao oot tao oot woo	VRIINILYQSNPYPSSEGTRQTRKNRRRW I K Itt agg att atc aaw atc ctc tac caa agc aat ccc tat ccc wca agc gaa ggc wcc agg caa rcc aga arg aat agg aga agg aga tgg	SEGTROTRKNRRRRRRRQRQIRAISERIL SAR tcc gag gga wca aga cag ara aac aga agg aga agg tgg agg gmg agg caa agg caa atc cic kcc atc tcc gag wgg att ctg	RARQRQIRAISERILST.CLGRSAEPVPLQL E HS W NF P aga gma aga cag agt crt kct att agc gaa wgg atc ctc agc amc tkc ctc ggc aga ycc gct gag cct gtg cct ctg caa ctg	STCLGRSAEPVPLQLPPLERLHLDCSEDCG
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Segment 6		Segment 7			Segment 8
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сукрсатустороуст	बटक टबेलु टबेब बेलुट टबेब लुलुट कटक पुष्रे	Ø		ace gaa ace gge gte gge mre eet cag att tyg gga gag tee age gyt rte	
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VPU ÖVERLAPPING SEGMENTS

## 45/216

Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
TPLEIIAIVAFIVALIIAIVWTIAYIEY S OR R	IIAIVVWTIAYIEYRKLLRQRRIDRLIKR L att mtc gct atc gtg tgg acc att gyg twt atc gaa tac arg aaa ctg ctc arg caa agg ara atc gat agg utc atc raa agg	KLLRQRRIDRLIKRTRERAEDSGNESEGD K ang ctc ctg ara cag aga arg att gac aga ctg att rag aga ayc aga gag aga gcc gaa gac tcc ggc aat gag tcc gag gga gac	RERAEDSGNESEGDTEELSTMVDMGNYDL RAL agg gaa agg gct gag gat agc gaa agc gaa ggc gat asa gaa gag ctc agc rca wtg gtc gac atg ggc aat tac gat ctg	EELSTWVDMGNYDLGVDNNL AL
M atg	Ctg	ᅜᄌᄌᇕ	E H &	工民品

HGURE 12 (Cont)

Segment 1	Segment 2		Segment 3		Segment 4		Segment 5		Segment 6	
KETQMNWPNLWKWGTLILGLVIICSAS R M M M	aaa gag aca cag atg aac tgg ccc aat ctg tgg arg tgg ggc aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc L I L G L V I I C S A S D N L W V T V Y Y G V P V W R	M M M E c wtg atc ctc ggc wtg gtg atk atc tgt agc gct agc gas aat ctg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg	WVTVYYGVPVWRDADTTLFCASDAKAH F F F	ப tgg gtc acc gtc tac tat ggc gtc ccc gtc tgg aga gas gct	TTLFCASDAKAHETEVHNVWATHACVP VD	acc aca ctg ttt tgc get agc gat gcc aaa gcc	V H N V W A T H A C V P T D P N P Q E I H L E N V T E	a gtg cat aac gtc tgg gct acc cat gcc tgt gtg cct acc gat ccc aat ccc caa gag xtt swc ctc gag aat gtg aca gag	NPOEIHLENVTENFNMWKNNMVEOMOE	aac cet cag gaa rte awt etg gaa aac gte ace gaa aac ttt aac atg tgg aaa aac rat atg gte gaa caa atg
>	ga gtg	gga acc	ᄓ	aac ctc	Ω F	gcc rmt	田	acc gaa	<u>д</u>	gac cct
R	e aga D		Z		A		[ <del>-</del> 4	gam ac	Д	aca ga
Σ	atg K	tgg	DF	g 6	D E	gam	MД	S)	E	ğ

ENV OVERLAPPING SEGMENTS

Segment 7		Segment 8		Segment 9
M V E Q M Q E D V I S I W D Q S I K F C V K Segment 7 D H I I I I I I I I I I I I I I I I I I	eg tgg gac caa agc ctc aag cct tgc gtc aag		go gto aco oto aao tgt aco aat goo aat otg	
1	atg gig gam cag aig cam gaa gac rit aic icc cig igg gac caa agc cic aag cci igc gic aag	LKPCVKLTPLCVTLNCTNANL	tec etg aaa eec tgt gtg aaa etg aca eec ete tge gte ace ete aac tgt ace aat gee aat etg	N C T N A N L I N V N at tgc aca asc gct asc ctc atc at gtg agt
E A A A E A A A	aat tto aat atg tgg aag aat rac at	DVISLWDQS I	gat rte att age ete tgg gat eag te	L T P L C V T L N ctc acc cct ctg tgt gtg aca ctg aa

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 1 AND 2	Д Д (1)	т н у С Прва	ccc aaa rtc wcc ttc gam ccc att ccc att cac tat tgc $r$ ct ccc gcc gga twc gct atc ctc aag tgt aac rat aag amm ttc aat ggc	FNGTGPCKNVSS	got ggo twi gco att otg aaa igo aat rac aaa ama tit aac gga aco gga oco igi amg aat gig ico aac gio cag igi aco cat ggo	TGPCKNVSSVQCTHGIKPVVSTQLLLNGSL	l aac gtc agc wcc gtg caa tgc aca cac gga atc	IKPVVSTQLLINGSLAEEEIIIRSENLTNN R att arg cot gtg gtc agc aca cag ctc ctg ctc aac gga agc ctc gcc gaa gaa gaa rtc rtt atc aga agc gaa and yt and str	DØ 364 375 37 117 37
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FIGURE 12 (Cont)

FIGURE 12 (Cont)

Segment 6 Segment 7 AEEEIIIRSENLTINNAKTIIVHLNESVEIN (V)(V)

FDV

QKV

gct gag gaa gat rtt rtc att agg tcc gag aat ytc aca rac aat gyc aaa acc att atc gtc cam ctc aac raa agc gtc gwg att aac 

Segment 1 Segment 2 Segment 3	Segment 5	Segment 6
G D I K D N W R S E L Y K Y K V V K I E P L G V  N M R  ggc rat ats ara gac aat tgg aga agc gaa ctg tat aag tat aag gtc gtg rag att rag ct ctg gga rtc  V V K I E P L G V A P T R A K R R V V E R E K R  gtg gtc raa atc raa cc ctc ggc rtt gcc cct acc ara gcc aaa agg aga gtg gtc sag aga gag aaa agg  R R V V E R E K R A V G I G A M I F G F L G A A  Q  aga agg gtc gtg saa aag gga aaa gcc gtc ggc mtt ggc gct atg wtt ytc gga ttc ctc ggc gct gcc  M I F G F L G A A G S T M G A A S I T L T V Q A  F L  atg wtc ytt ggc ttt ctg gga gcc gct ggc tcc acc atg ggc gct gcc tcc ats aca ctg aca gtg caa gcc	ASITLTVQARQLLSGIVQQQSNLL M gct agc atk acc ctc acc gtc cag gct agg cwa ctg ctc agc gga atc gtc cag caa cag arc aat ctg ctc	IVQQQSNLLRAIEAQQHLLLQLTVW M att gtg caa cag caa art aac ctc ctg agg gct atc gaa gcc caa cag cat mtg ctc cag ctc acc gtc tgg
as as 50 g	U	E E
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H H gg K h h g	C) B	다 <sup>#</sup>

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 3,4 AND 5

Segment 7	Segment 8	Segment 9	Segment 10	Segment 11	Segment 12
RAIEAQQHLLOLTVWGIKQLQARVLAVERY M aga gcc att gag gct cag caa cac wtg ctg caa ctg aca gtg tgg ggc att aag caa ctg caa gcc aga gtg ctc gcc rtt gag aga tac	GIKQLQARVLAVERYLKDQKFLGLWGCSGK I gga atc aaa cag ctc cag gct agg gtc ctg gct rtc gaa agg tat ctg aaa gac caa mag ytt ctg gga mtc tgg ggc tgt agc gga aag	LKDQKFLGLWGCSGKIICTTAVPWNSSWSN QL I ctc aag gat cag maa ytc ctc ggc mtt tgg gga tgc tcc ggc aaa mtc att tgc aca acc rmt gtg cct tgg aac agc wcc tgg tcc aac	IICTTAVPWNSSNKSLEEIWNNMTWMEW L F D IQ mtt atc tgt acc aca xmc gtc ccc tgg aat tgg agc aat aag tcc ytc gaa gag att tgg rat aac atg acc tgg ats saa tgg	KSLEEIWNNMTWMEWEREISNYTNQIYEIL F D IQ aaa agcytt gag gaa atc tgg rac aat atg aca tgg atk sag tgg gag agg att agc aat tac aca arc cwa atc tat rag att ctg	EREISNYTNOIYEILTESONOODRNEOELL SLKD gaa agg gaa atc tcc aac tat acc art cwg att tac raa atc ctc acc gaa agc caa aac caa cag gat agg aat gag maa gas ctc ctg

Segment 13	Segment 14	Segment 15	Segment 16	Segment 17	Segment 18
TESONOODRNEQELLELDKWASLWWFDIT Seg KDA aca gag tee eag aat eag eaa gae aga aae gaa mag gam etg ete gmg ete gae aaa tgg get age ete tgg aat tgg ttt xae att age	ELDKWASLWWFDITNWLWYIKIFIMIVGG A gma ctg gat aag tgg gcc tcc ctg tgg aac tgg ttc rat atc wcc aa8 tgg ctg tgg tac att aag att ttc att atg att gtg gga ggc	NWLWYIKIFIMIVGGLIGLRIVFAVLSIVN Seg K Aam tgg ctc tgg tat atc aaa atc ttt atc atg atc gtc ggc gga ctg rtt ggc ctc agg att rtc ttt gcc gtc ctg tcc atc rtt aac	LIGLRIVFAVLSIVNRVRQGYSPLSFQTLLSSE V I T Corre 99a ctg aga atc rt ttc gct gtg ctc agc att rtc aat a99 gtc a99 caa 99c tat agc cct ctg tcc ttc caa acc ctc myc	RVRQGYSPLSFQTLLPAPRGPDRPEGIEES <sub>et</sub>	PAPRGPDRPEGIEEEGGEQDRDRSVRLVSG Sel LGR cot goc cot agg gga coc gat agg cyg grg rga atc gaa gag gaa ggc ggc ggg cra grc aga agc gtc agg ctc gtg art ggc

agg rtt atc gaa gtg gyt cag Ü O O) G L R R G Q a ggc ctc crg aga g Ø Ī4 tgc ctc tgg ggc cwg gaa ctg aaa awc tcc gcc rtt agc ctc ctg aat gcc aca < > Ы Z Н  $\alpha$ U ď > ctg aga arc ctc aac ctc ctg cwa Д z 闰 Ы Ы Н S ט ctg ara R R Н Н ĸ Ŋ 니 Z Н 24 П L G H S S L
R
sete 990 cut ago too o gat gac ytt > H Д 되도 Д Н ď Д Д Ω ⋈ kgg t.99 × വ ⋈  $\alpha$ EALKY G G gaa gsc ctc aag t aga ctg cte gee HZ ď Ы ace get ate get gtg get × Ы П R tat cac gaa ctg À Ы > K 出 ď 闰 × 闰 R I V E
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Agg ayt gtg g tto tgg ᇰᆸ H ⋈ ഥ Ŋ ctg ttt **99a** ტ ტ ט ď Œ **a**99 ctg gtc arc 3 民 Н S S Н A A ]
V
syc get ctg tgt R Q E tee etg ete aac get  $\mathbf{c}$ ø > П П z Н aga **888** gat gac ctc agg art Ö П O(Z H 24 gtg R K # Ы >  $\alpha$ Ы F F att oto Ы ល Н Ŋ Н Ω Ø R toc A. А Ø А 田瓦品 × ഗ ρ4 ⋈ 吆 ម្ភិធ gga O X HZ Ø Н A L I G L I get ctg Q R E ¥ Н ĸ Н 耳 Ы K Н 闰 H W 闰 闰 Ö × 闰 tgg O L S tt ≊ Ö [T, ល >

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Segment 25		Segment 26	
OI	rtc att gag gtc gyc caa agg gct kgg aga gcc att ctg mat atc cct asa aga atc aga cag		
24	aga		
н В	atc		
p <del>c</del>	808		
VIEVAQRAGRAILHIPRR I V W N T	. B		
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NEF OVERLAPPING SEGMENTS

## 55/216

Segment 11 Segment 7 L W V Y H T Q G F N N  $\times$  V V N  $\times$  Ctg tgg gtg tat mac aca cag gga two tgo ttt aag ctc gtg cct gtg gat ccc gtc Н NNCLLHPMSQHGMEDEEREV ICL aat aac tgt ctg ctc cac cct ats rgt cwg cat ggc atg gaa gac gaa gas aga gag 民 Д Ы  $H \not\vdash >$ บ Ö Д Z twt tto cot gae tgg cas aat tae aea eee gga eee Z 闰 Ы Ö gtg gaa gag ryc aac raa ggc × Ŋ Д 以区 Ŀ Η × O Z ctg gat tat occ etc acc ttt gge tgg НΚ Д z ⋈ HO Ы Ö 闰 att [±, Н ≊ 闰 caa gas > 田口 Д Н gaa O Д Ы 闰 agg PRI S cct ags വ് ſτι Д K Eq >4 × X Or g 990 tgt ttc aaa ctg gtc ccc gtc gac rya agg А 民 Ö too CBB > ט വ Ø EGLVYS
D I cag gaw atc ctc gat ctc tgg gtc tac mat acc ρι  $\vdash$ Ö act > z H Z p, gga gag Н 闰 × Ö Caw aac tat acc cct > Д × Ö E I N K G
A E Z H ſτι cta Ы Ц ⋈ Ö 990 99a tgg ტ Д Z ≊ П HO Ġ Ü tto aag н 3 ſΞι 团 gaa ctg aca 臣(口) 闰 А Н > Ы Ø 闰 ρų aga ស ល ឆ្នុំ ttt Ы ĸ Д [I,

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Segment 12	Segment 13
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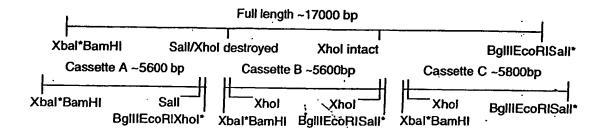
The	The Genetic Code- First and Second	Code-	First	and		osc Fr	Most Frequently Used Codons	980	a Codons											
AAIA	ಡಿಡಿದ/ಅಲಾ	R Arg	AGG/AGA		N ABD AAC/AAT	D Asp	D Asp GAC/GAT	ပ်လို့	c cys tgc/tgt gln cag/caa	gln	CAG/CAA	8 G1u	GAA/GAG	g gly	GGC/GGA	H His	CAC/CAT	I	ATC/ATT	
The	Genetic Code- First and Second	Code-	First	and		ost Fr	Most Frequently Used Degenerate Codons	. Иве	d Degene	rate	Codons	For	TWO OF	More	More Amino Acids	cids				
TWO	TWO BASES AT A SINGLE POSITION	r A SI	NGLB PC	SITI	NO															
8	GMC/GMT	ž	AKT/		RAC/RAT	S	RAC/RAT	3	TGS/TGK	క్ష	CRG/CRA	ß	GAS/GAM		KGG/	Ä	MAC/MAT	ΣΗ	ATS/ATK	
A	GMG/GMA	ž	WGG/YGG		MAC/MAT	ă	GMC/GMT	ฮ	YGC/YGT	O	SAG/SAA	g	SAG/SAA		GRC/GRT	县	SAC/SAT	Z	AWC/AWT	
2	GSC/GST	2	YGC/YGT	N	AWC/AWT		GAS/GAM	8	KGC/KGT	ö	CAM/CAW	Ø	GMG/GMA	ຍູ	KGC/KGT	2	CAM/CAW	I.F	WTC/WTT	
AP	SCC/SCI	8	CRG/CRA		AAS/RAM	8	GRC/GRT	ť	TKC/TKT	강	CWG/CWA	ğ	GRG/GRA		GRG/GRA	¥	CRC/CRT	ñ	AKA/	
ą	KCC/KCT	2	CRC/CRT		ARC/ART	HO	SAC/SAT	8	WGC/WGT	Š	MAG/MAA	X	RAG/RAA		GSC/GST	Ξ	CWC/CWT	H	MTC/MTT	
FK	RCC/RCT	¥	ARG/ARA		AMC/AMT	מא	KAC/KAT	ដ	TRC/TRT	g	CMG/CMA	ā	GWG/GWA		SGC/RGA	Ä	CMC/CMT	18	AKC/AKT	
¥	GYC/GYT	RI	AKA/		WAC/WAT	à	GWC/GWT								RGC/RGT	¥	YAC/YAT	H	AYC/AYT	
	•	2	SGC/RGA												GKG/GKC		•	감	RTC/RTT	
		RP	CSC/CST															X	AWA/	
		RT	ASA/ASG																•	
		RL	CKG/CKC																	
		23	MGC/MGT	_																

FIGURE 13

e was the company of the company of

		t s			0 4466000	59/216	
		crg/crc			MYG/WTG TKG/ TYG/TYA CWC/CWT YTC/MTT MTC/MTT CYC/CYG SYG/SYC CKG/CYG	39/210	
		r Leu			re certa com		
		GTG/GTC			RTG/GWT GWG/GWT GWG/GWT KTC/KTT RTC/RTT GYC/GYT GYC/GYT STG/GKC		
		v Val	Acids		W		
		y Tyr TAC/TAT	More Amino Acids		WAC/WAT TRC/TRI TRC/TRI TWC/TWI TWC/TWI TWC/TWI		
		¥ţ	More		XX		
		199/	TWO Or		WGG/YGG KGG/ TSG/ TKG/ TGS/TGK	•	
		a ti	For		W W W W W W W W W W W W W W W W W W W		
		T Thr ACC/ACA	e Codons		AYG/ AMC/AMT AMG/AMA AYC/AYT RCC/RCT ASC/MCC ASC/MCC		
	81	Tabr	nerat		ME KET KET KET KET KET KET KET KET KET KE		1
	The Genetic Code- First and Second Most Frequently Used Codons	AGC/TCC	Frequently Used Degenerate Codons		TSG/ ARC/ART TYG/TYA WGC/WGT TWC/TYT TWC/TYT ARC/AKT KCC/KCT KCC/KCT KCC/KCT	MGC/MGT	ElCime 13
	ly u	Ser	ly u		S S S S S S S S S S S S S S S S S S S	ස	
	Frequent	בככ/ככב	Frequent		CMG/CMA CMC/CMT SCC/SCT CSC/CYG YCC/YCT MCC/MCT		
	lost	Pro			P P P P P P P P P P P P P P P P P P P		
,	Second N	TTC/TT	Second N	NO	TKC/TKT WTC/WTT YTC/YTT TWC/TWT KTC/KTT		
٠	and	P Phe	and	SITI	P P P P P P P P P P P P P P P P P P P		
i	- First	ATG/	Genetic Code- First and Second Most	BASES AT A SINGLE POSITION	AKT/ ATB/ATK MTG/WTG AWG/ AYG/ RTG/	19 CH OH O	
,	Code	A aet	Code	2 K	<b>ARBARS</b>	# 99999 6 FF6F6	
	Genetic	AAG/AAA	Genetic	BASES AT	AWG/AAM AAS/AAM AAG/WAA RAG/RAA ARG/AXA AMG/AWA AWA	Single letter  R = A or G  K = G or T  S = C or G  W = A or T  H = A or C or  B = C or G or  V = A or C or  N = A or C or  O = A or C or	
ī	The	rys Fys	The	TWO	<b>£ 5 5 5 5 7</b>		

FIGURE 13 (cont)



Full length construction after cloning the cassettes into pBS Sites marked with a \*\*\* are in the pBS MCS

## Cassette Extras (Can be removed from cassette ends)

A (37bp) BamHl/Kozak S		Stop Bglll	EcoRi
5' gc ggatccacc B (43bp) BamHl/Kozak S		tga agato Stop Bglil	et gaatte ge 3' EcoRl
5' gc ggatccacc C (37bp) BamHl/Kozak	atg ctcgagctcgag		t gaatte ge 3'
5' gc ggatccacc			t gaatto gc 3'

FIGURE 14

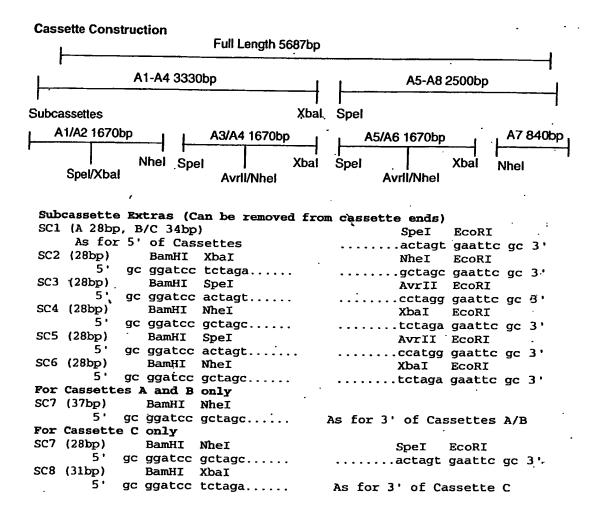


FIGURE 14 (Cont)

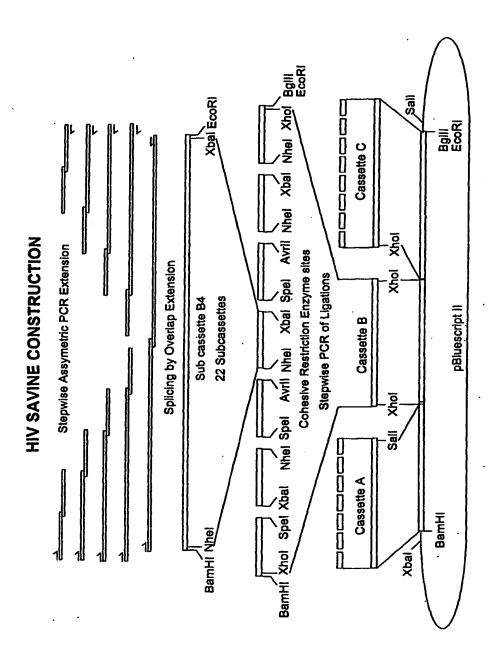
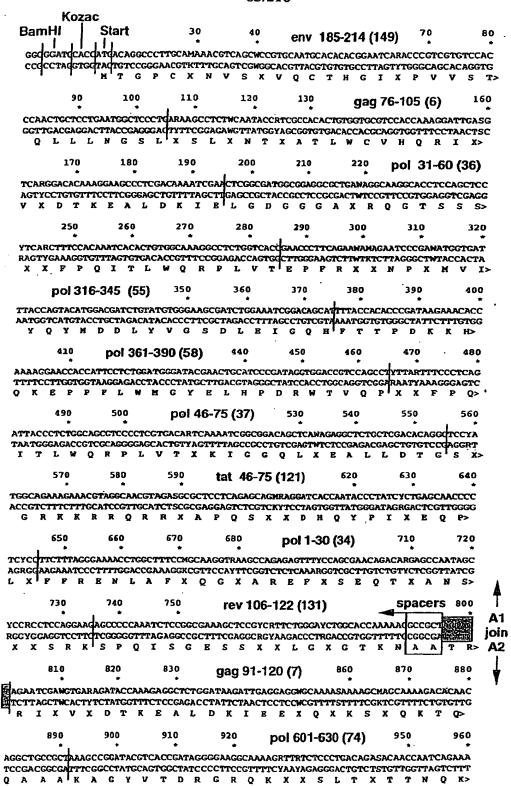


FIGURE 14 (Cont)



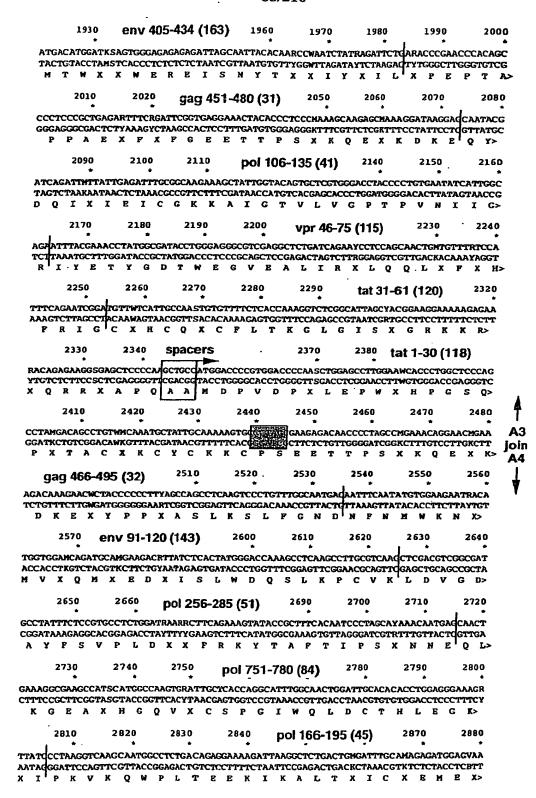
### FIGURE 15

			_				
970	980	990	1000	1010	env 40	6-75 (140)	1040
ACCGAACTGCAW	GCCATTCAM	* :AMGCCRMTAC	· CACACTGTTT	* TGCGCCAGCG	ATECCANAGE	CYATGASACAG	AGGTCCA
TGGCTTGACGTW							
T E L X		XAXT					E V H>
. T E B A	A . A		1 4	C	, , , ,		2 1
1050	1060	1070	1080	1090	pol 76	5-105 (39)	1120
•	•		*	*	-	• •	*
CAATGTGTGGGCC							
GTTACACACCCGG						L P G X	
NVWA	THA	C V P. A	UUT	V L E		PGA	W K.
1130	1140	1150	1160	1170	1180	1190	1200
•	*	*	*1	•	·	•	
CTAAGATGATTGG							
GATTCTACTAACC							
PKMIG	GIG	G P I	K V R'X	IGP	E N P	YNTP	X F>
pol 196-2	25 (47)	1230	1240	1250	1260	1270	1280
pui 190-2	25 (47)	•	•	• •	•	•	•
GCTATCAAGAAAA	AGGACTCCAC	CANATGGAGA	AAGCTCGTGG	ATTTCAGE RT	PAGGATTATC	AAWATCCTCTA	CCAAAG
CGATAGTTCTTTT	TCCTGAGGTG	GTTTACCTCT	PTCGAGCACC	TAAAGTCT YA	NTCCTAATAG	TTWTAGGAGAT	GGTTTC
AIKK	K D S T	KWR	K L V	D P R X	RII	XILY	Q S>
1290	rev 16-4	5 (125)	1320	1330	1340	1350	1360
*		• •	•	•	*1	*	*
CAATCCCTATCCT							
GTTAGGGATAGGAT							
N P Y P	SSE	GXRQ	X R X	NRRE	R W'G	G E X	X R>
1370	1380	env 525-5	EA (474)	1410	1420	1430	1440
1370	*	elly 323-3	134 (171)	1110	*	*.	*
ATAGGTCCGTGAGA	CTGGTCARC	GATTCTYAGO	CCTCCCCTGC	GACGATCTGA	GAARCCTCTC	CCTCTTCGAM	AACCTC
TATCCAGGCACTCT	GACCAGTYG	CTAAGARTCG	GGAGCGGACC	CTGCTAGACT	CTTYGGAGAC	GGAGAACTK	PTGGAG
D R S V R		G F X A					N L>
	_						
1450	1460	1470	env 31-6	0 (139)	1500	1510	1520
•	*	*			•	•	
TGGGTCACCGTCTA							
ACCCAGTGGCAGAT							
WVTVY	A C A	PVWI	ххх	TTL	FCA	SDAK	·A X>
cnacore		1550	7560			1590	1600
spacers		1550	1560	rev 1-30	(124)	1390	1000
CCTCCCATGCTG		~			*****		TC AGT
GCGACGGTACCGACG							
1 1						XILY	
	, , , ,	* 1 0			**		*
1610	1620	1630	1640	1650	vif 16-4	(101)	1680
*		•	•	*	VII 10-4.	, (101)	
CCAACCCTTACCCTT	COSCER	TGARAATCAGA	ACCIGGAAS	AGCCTGGTCAA	GCATCACAÍN	YACATCTCCA	<sub>AGAAA</sub> A
GGTTGGGAATGGGAA	COEFFICIE	ACTYTTAGTCT	TGGACCTTS	CGGACCAGTT	CGTAGTGTAG	RTCTAGAGGT	тсттт іО
				SLVK		XIS	
1690	1700	1710	1720	1730	1740	1750	1760
	*	*	*	•	•	•	• 1
CCAAWGGCTGGTTC	TATAGGCATO	CACTUTGASCA	CTCCCAGSTC	CTGARTCAGA	TTATCGAAVA	GCTCATCAAA	AAGGA '
GGTTWCCGACCAAG							
AXGWF							K E>
				· •			
pol 661-690	(79)	1790	1800	1810	1820	1830	1840
hot oo 1-020	(10)	•	* ,	•	•	•	•
ARGGTCTACCTAKC	ATGGGTACCA	GCCCACAACC	GAATCECACA	AACCAAAGAG	CTCCAGAAMC	AGATTMYCAA	ATCC
TYCCAGATGGATMG							
XVYLX							
	•		_				
1850	pol 916-94	15 (95)	1880	1890	1900	1910	1920
= =:		··· ()	•	٠,	•	•	*
AAACTTTAGGGTCT	ACTATAGGGA	TAGCAGAGAC	CTMTCTGGA	AGGGACCGAA	AAGCYTTGAG	GAAATCTGGRA	CAAT
TTTGAAATCCCAGA							
						RTWY	

FIGURE 15 (Cont)

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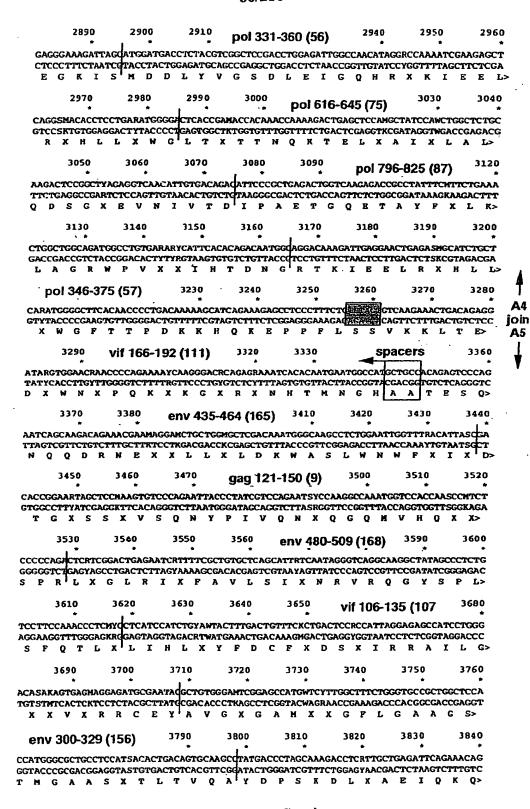
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FRGURE 15 (Cont)

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## 阿姆斯克斯克 15 (Cont) SUBSTITUTE SHEET (RULE 26)

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3920

3890

3970

4050

4290

4370

4450

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4610

4690

4770

4700

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4790

4800

3900

3880

3960

pol 301-330 (54)

GGTCAGGRTCAGTGGACATWTCAGATTTWCCAAGAGCCTTTCAAAAAAGGAACCGTCCTGGTCGGCCCTACACCCGTCAA

nef 136-165 (188)

4200

4280

4360

4440

4520

4600

4680

4760

TATGGCCACTCTCTGACCGTSGAGCCGGTWCCGCAGTCGTAACTCACCTCTTTTCCCGTTTCCCGACTCCTATCGCCG
H T G E R D W X L G X G V S I E W R X R E R A E D S G>

GATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGAWGCCAGACTGRTTATCARAACCTATTGGGGACTGC CTACTTCCTAACGTGACTCTCTGTCCGATTGAAAGACCCTTTCCTWCGGTCTGACYAATAGTYTTGGATAACCCCTGACG

3870

4110

4190

4270

4350

4430

4510

4590

4670

4750

pol 121-150 (42)

4020

4100

4180

4260

4340

4420

spacers

4660

pol 466-495 (65)

3930

4010

4170

4250

4650

vif 61-90 (104)

CCAGTCCYAGTCACCTGTAWAGTCTAAAWGGTTCTCGGAAAGTTTTTCCCTTGGCAGGACCAGCCGGGATGTGGGCAGTT
G Q X Q W T X Q I X Q E P F K N G T V L V G P T P V N> 3980 3990 4000 CATCATCGGAAGGAACHTGCTGACACAGHTTGGCYGCACCCTCAACTTTCCCATTAGGAAAGGCAGCCCTGCTATCTTTC GTAGTAGCCTTCCTTGKACGACTGTGTCKAACCGRCGTGGGADTTGAAAGGGTAATCCTTTCCGTCGGGACGATAGAAAG I I G R N X L T Q X G X T L N P P I S X G S P A I F> 4060 4070 4080 AGTCCAGCATGHCAMAGATTCTGGAGCCTTTTAGGAWAMAAAACCCTGASATGGTCATCTATCAGTA ACCTOTO TCAGGTCGTACKGTKTCTAAGACCTCGGAAAATCCTWTKTTTTGGGACTSTACCAGTAGATAGTCATAGGGAGAC Q S S M X X I L E P F R X X N P X M V I Y Q Y 4150 4140 ACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGSGAAGTGGAAGAGRYCAACRAGGGCGAAAACAATTGCCT TGTAAGCCTACCACAAAGTTTGACCAGGGGCACCTGGGGTCSCTTCACCTTCTCYRGTTGYTCCCGCTTTTGTTAACGGA V D P X E V E E X N X G E N N C L> 4230 4240 pol 271-300 (52) CCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCAYCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCC GGADAATCCTTTATGTGTGGGAAATGGTAAGGGAGGTRGTTATTGCTTTGGGGACCGTAATCCATAGTCATATTGCAGG PRKYTAFTIPSXNNETPGIRYQYNV> env 315-344 (157) pol 451-480 (64) GTCCAGCAACAGARCAATCTGCT4GHGGAGAATAGGGAAATCCTCARAGAGCCTGTGCATGGGGTCTACTACGATCCCTC CAGGTCGTTGTCTYGTTAGACGACKCCTCTTATCCCTTTAGGAGTYTCTCGGACACGTACCGCAGATGATGCTAGGGAG VQQQXNLLXENREILXEPVHCVYYDPS vpu 61-81 (136) GTTCCTAGACYAGCGACTTYAGGTTTTCGTTCCCTSTCTCCTTGACAGGYGCNACCACCTATACCCTTTGATGCTGGAGC
K D L X A B X Q K Q G X B E L S X X V D H G N Y D L> 4560 vpr 61-90 (116) GAGTGGACAATAACCTGCCGCTATTAGAAYCCTGCAACAGCTCMTGTTCRTTCACTTTAGGATTGGCTGCCRGCACTCC CTCACCTGTTATTGGACGGCGGTTATCTTRGGACGTTGTCGAGKACAAGYAAGTGAAATCCTAACCGACGGYCGTGAGG G V D N N L A A I R X L Q Q L X P X H P R I G C X H S> gag 406-435 (28) 4640 aggattggcatchyccgtcagagaagggscag/gctcccaggaaaaagggatgctggaagtgtgccaragagggcacca TCCTAACCGTAGKRGGCAGTCTCTCCCSGTCTCGAGGGTCCTTTTTCCCTACGACCTTCACACCGTYTCTCCCTGTGT
R I G I X R Q R R X R A P R K K G C W K C G X B G H Q APRKKGCWKCGXBGHQ> 4720

FIGURE 15 (Cont)

**SUBSTITUTE SHEET (RULE 26)** 

**A5** ioin **A6** 

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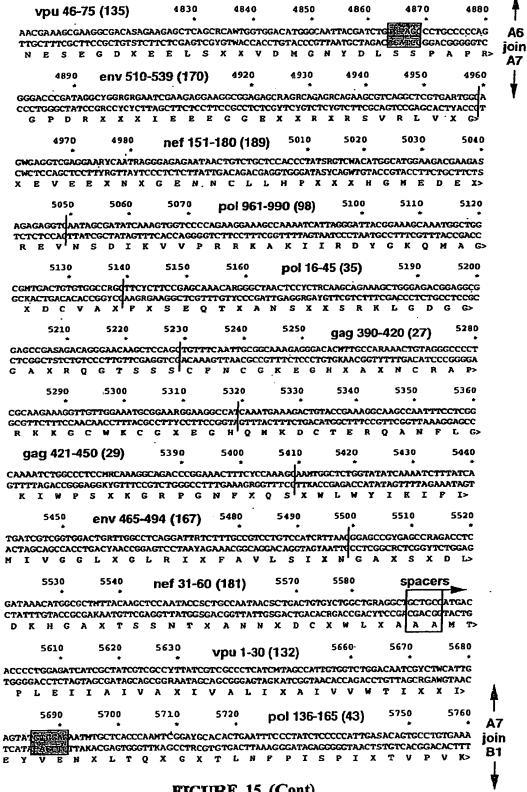
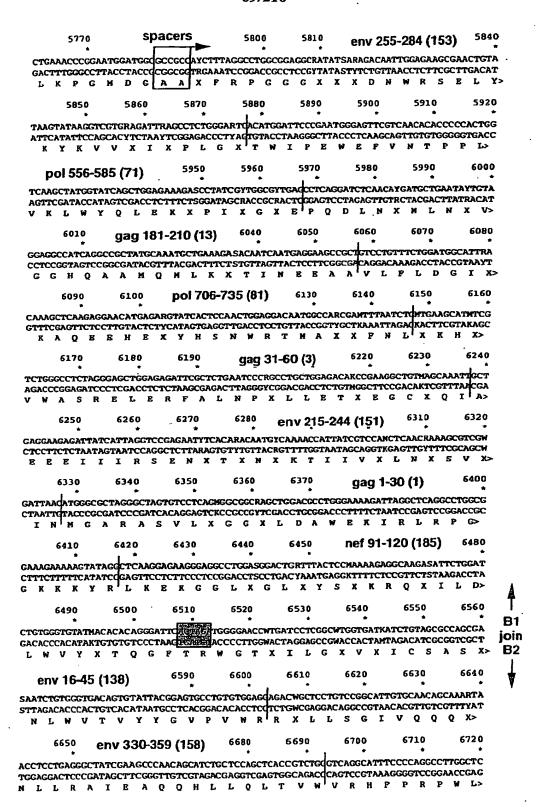


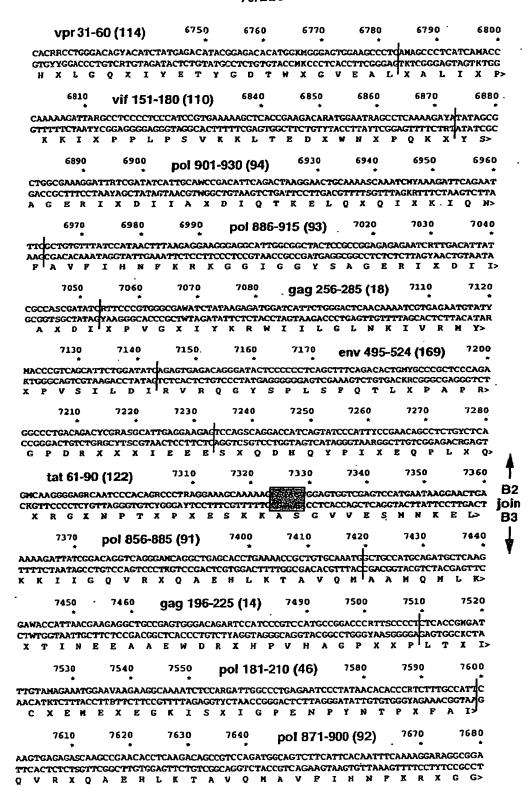
FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)



## FIGURE 15 (Cont)

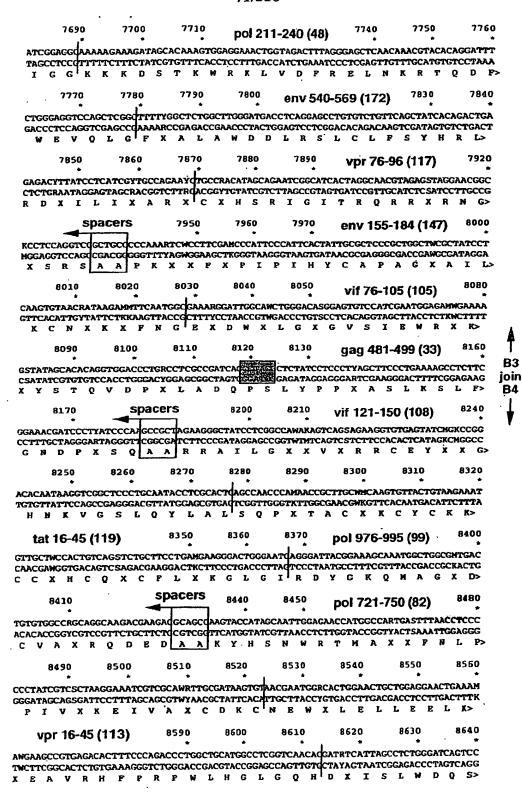
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## REGURE 15 (Cont)

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# FIGURE 15 (Cont) SUBSTITUTE SHEET (RULE 26)

B4 join B5

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8650	env 106-	-144 (144)	8680	8690	8700	8710	872
CTGAAACCCTGT	GTGAAACTGAG	ACCCCTCTGC	GTCACCCTC	AACTGTACCA	ATGCCAATCT	- HINGAAGAGHT	'ACTCCA(
GACTTTGGGACA L K P C	CACTTTGACTG	TGGGGAGACG	CAGTGGGAG	TTGACATGGT:	PACGGTTAGA	INWCTTCTCKA	TGAGGT
L K P C	V K L 1	PLC	V T L	NCT	VANL	'х к х	Y S 1
8730 *	8740 •	vif 91-12		8770 •	8780	8790	8800
CCAAGTGGACCCC GGTTCACCTGGGC	GRTCTGGCTG	ACCAWCTGAT:	rcacctcca herecae	CTATTTCGATT	GCTTTKCCGA	TAGCRCAATC	CATCCCA
Q V D P	X L A	D X L I	H L H	Y F D	C P X D	S X I	
8810 *	8820 *	8830	nef 166-	195 (190)	8860	8870 *	8880
TSRGCCWACACGG							
ASYCGGWTGTGCC X X X H G						ACCGAGMGTCC L A X R	
8890	8900	8910	8920	pol 151-	180 (44)	8950	8960
GCT CCTA	ICGAWACCGTC	CCCGTCAAGC	TCAAGCCTG	GCATGGACGG!	CCCAAAGTG	AAACAGTGGCC	CCTCAC
CGARLETT GGAT	AGCTWTGGCAG IXTV	GGGCAGTTCG P V K	AGTTCGGAC L K P	CGTACCTGCC1 G M D G	GGGTTTCACT	TTGTCACCGG	GGAGTG L T>
					, K 4		15 17
8970	8980 .*	8990	9000	9010	gag 436-	465 (30)	9040
CGAAGAGAAAATCA	AAGCGATTTG	GCCTAGCMRCI	AAGGGAAGG	CTGGCAATTT	CCYGCAGTCC	ARGCCTGAGCC	TACCG
GCTTCTCTTTTAGT E E K I	TTCGGTAAAC K A I W	CGGATCGKYGT PSX	TCCCTTCC	GACCGTTAAA P G N P	GGRCGTCAGG	TYCGGACTCGG	ATGGC
					A Q 5		. 1>
9050	9060	9070	9080	9090	vif 31-60	(102)	9120
CACCCCCAGCCGAG							
GTGGGGGTCGGCTC A P P A E	TYGAAAYCTAA X P X F	GCCGTAATCG	TTTTTCCGA	TTSCCTACCA	ULATGICICION	GTAAWGCTWT	CGGYT S X>
				7 G W 1	IKB	пка	5 A
9130	9140	9150	9160	9170	9180	9190	9200
CACCCTAAGGTCAG							
GTGGGATTCCAGTCC				CTGGCGAACGG T A C			
	-		U A A	TAC	Q G V G	, G P A	н к>
gag 346-37	75 (24)	9230	9240	9250	9260	9270	9280
AGCCAGGGTACTGGCAGAGGCTATGTCCCAGGYGANCHACGCTAACATTCCTCCCATTGTGSCCAAAGAGATTGTGGCAN TCGGTCCCATGACCGTCTCCGATACAGGGTCCRCTKGKTGCGATTGTAAGAGGGTAACACSGGTTTCTTCTAACACCGTW							
ARVLA	EAM	s Q x x	XAI	IPP	XVI	KEIV	.A>
9290	pol 736-76	5 (83)	9320	9330	9340	9350	9360
RCTGTGACAAATGCC	AGCTCAAGGGT	GAGGCTATKC	ACCGACAGG	* ማርያልቦማርዋልርነ	Capacasa	* CCAWPAAGAPA	CRCT
YGACACTGTTTACGG	TCGAGTTCCCA	CTCCGATAMG	TECCTETCO	ACYTGACATCO	GGZAGGCTC		
хсркс	Q L K G	EAX	н с б	v x c s	P'S E	G X R Q	X>
9370	9380	rev 31-60	(126)	9410	9420	9430	9440
AGGARGAACAGACGT							
TCCTYCTTGTCTGCA R X N R R							
9450	9460	9470 <b>Q</b>	ag 226-2	55 (16)	9500	9510	9520
GGAACCCAGAGGCTC	TGACATTGCCG		_	•	* CAMCCAMCAC	• ••••••••••••••••••••••••••••••••••••	-cale
CCTTCGGTCTCCGAG	CTGTAACGGC	CATGGTGTTC	TGTGACGT	CTCGTTTAGC	STACCTACTG	TTYGTTAGGGG	GAY
EPRGS	DIA	G T T S	T L Q	E Q I	X W M T	X N P	βĄ
9530	9540	955 <u>0</u> 9	9560	pol 841-87	0 (90)	9590 9	600
RCATTMAGCAAGAGTT	TGGCATTCCC	- PATAACCCTCA	•	-		AAGAGCTCAAG	:AAA
YGTAAKTCGTTCTCAA	ACCGTAAGGG	atattgggagt	CACCGTCCC	GCAGCACCTT	<b>ICGTACTTGT</b>	TTCTCGAGTTC	TTT
XIXQEF	GIP	Y N P C	so	VVE	S M N	KELK	K>

# FIGURE 15 (Cont)

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**B**5

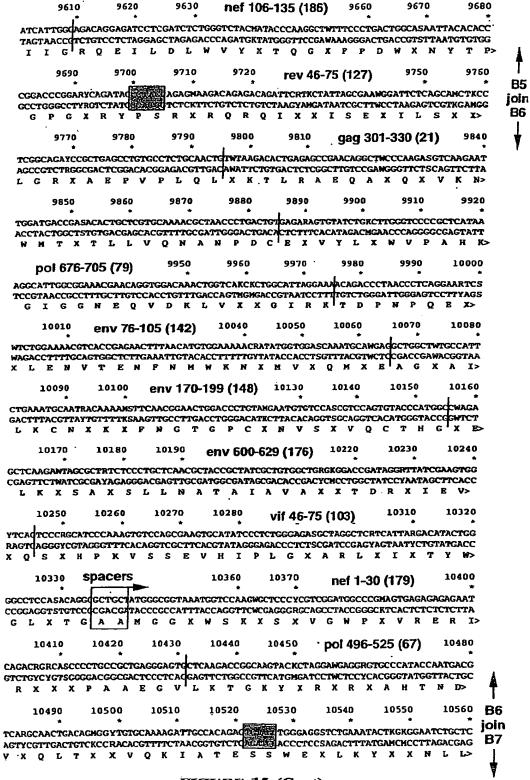


FIGURE 15 (Cont)

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10620 ' 10630 10640 10590 10600 10610 env 585-614 (175) CWGTACTGGGGCCWGGAACTGAAAAWCTCCGCCRTCAGCCTCCTGAATGCCACAGCQATTSWGCTGCCTGAGAAAGAWAG GWCATGACCCCGGWCCTTGACTTTTWGAGGCGGYAGTCGGAGGACTTACGGTGTCGQTAASWCGACGGACTCTTTCTWTC X Y W G X E L X X S A X S L L N A T A I X L P E K X S> 10700 10710 10720 10690 10650 pcl 391-420 (60) 10680 CTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCATCCCAGATTTACSCCGGAAGAGCCATTGAGG GACCTGGCAGTTGCTATAGGTTTTCGAGCACCCTTTCGAGTTGACCCGTAGGGTCTAAATGSGGCCTTCTCGGTAACTCC W T V N D I Q R L V G K L N W A S Q I Y X G R A I E> 10790 10800 10740 env 345-374 (159) 10770 10780 10730 CTCAGCAACACWTGCTGCAACTGACAGTGTGGGGCATTAAGCAACTGCAAGCCAGAGTGCTCGCCRTTGAGAGATACTC CACTCCTTGTCHACGACGTTGACTGTCACACCCCGTAATTCGTTGACGTTCGGTCTCACGAGCGGYAACTCTCTATCGAG A Q Q H X L Q L T V W G I R Q L Q A R V L A X E R Y L> pol 631-660 (76) 10860 10870 10830 10810 10820 GCCTCCAGGATAGCGGATYGGAAGTGAATATCGTCACCGATAGCCAATACGCTCTAGGCATCATTCWGGCTCAGCCTGA CGGGAGGTCCTATCGCCTARCCTTCACTTATAGCAGTGGCTATCGGTTATGCGAGATCCGTAGTAAGMCCGAGTCGGACT ALQD S G X E V N I V T D S Q Y A L G I I X A Q P D> 10910 10920 env 420-449 (164) 10950 10960 10890 10900 CARAAGGGAAAGGGAAATCTCCAACTATACCARTCWGATTTACRAGATCCTCACCGAATCTCAAAATCAACAGGATAGGA GTYTTCCCTTTAGAGGTTGATATGGTYAGWCTAAATGYTCTAGGAGTGGCTTAGAGTTTTAGTTGTCCTATCCT X S E R E I S N Y T X X I Y X I L T E S Q N Q Q D R> 11000 11010 env 285-314 (155) 10980 10990 10970 ATGAGHAAGASCTCCTGGCTCCCACAARGGCTAAGAGAAGGGTCGTGSAAAGGGAAAAGCGTGCCGTCGGCHTTGGCGCT TACTCRITCTSCAGGACGAGGGGTGTTYCCGATTCTCTTCCCAGCACSTTTCCCTTTTCGCACGGCAGCCGKAACCGCGA N E X X L L A P T X A K R R V V X R E K R A V G X G A> pol 91-120 (40) 11060 11070 11080 11090 11050 ATGWTTYTCGGATTCCTCGGCGCTGCC AAACCCAAAATGATCGGGGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGA TACWAARAGCCTAAGGACCGCCCACGGTTTGGGTTTTACTACCTCCGTAACCTCCGAAATAGTTTCAGTCCGTCATACT
M X X G F L G A A K P K M I G G I G G F I K V R Q Y D> 11190 11180 11150 11160 11170 CCAAATCHTTATCGAAATCTGTGGAHASAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGYCGCTAGGA GGTTTAGKAATAGCTTTAGACACCTKTSTTCCGATAGAGGATGGTATCCGAGTCCCTAAAGTAAGACTAGCRGCGATCCT QIXIEICGXKAISYHRLRDPILIXAR> 11270 env 555-584 (173) 11230 11240 11250 11260 YTGTGGAACTGCTCGGCCRTAGCTCCCTGARAGGCCTCCRGAGAGGGACACTGAATGCCTGGGTGAAAGTGRTTGAGGAA RACACCTTGACGAGCCGGYATCGAGGGACTYTCCGGAGGYCTCTCCQTGTGACTTACGGACCCACTTTCACYAACTCCTT X V E L L G X S S L X G L X R G T L N A W V K V X E E> 11350 11360 11320 11330 11340 11290 gag 151-180 (11) AAGGSATTCARTCCCGAAGTGATTCCCATGTTTWCCGCTCTGTCCGAGGGAGCCACAGTGAGGAACACACACCGCTAA TTCCSTAAGTYAGGGCTTCACTAAGGGTACAAANGGCGAGACAGGCTCCCTCGGTGTGAGSGTCTCGTTGTGTSGGCGATT **B7** join K X F X P E V I P M P X A L S E G A T L E S N T X A N> C<sub>1</sub> 11410 11420 11430 11380 11370 nef 46-75 (182) CANTSCCGATTCCGYGTGGCTGRAAGCCCAGGAAGAGGAAGRAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCK GTTASGGCTAACGCRCACCGACYTTCGGGTCCTTCTCCTTCYTCACCCTAAAGGACACTCTGGGGTTCACGGATCTCGGM N X D C X W L X A Q E E E X V G F P V R P Q V P R A> spacers 11490 11450 env 630-651 (178) GGAGGGCTATCCTCMACATTCCCASGAGGATTAGGCAAGGCYTTGAGAGAGCCCTCCTAGCCGCGGAATGGGATAGGRTT CCTCCCGATAGGAGKTGTAAGGGTSCTCCTAATCCGTTCCGRAACTCTCTCGGGAGGATCGGCGGCTTACCCTATCCYAA X R A I L X I P X R I R Q G X E R A L L A A E W D R X>

FIGURE 15 (Cont)

```
11600
                                                        11590
                                               11580
                                       11570
                    gag 211-240 (15)
             11540
    11530
CACCCTGTGCACGCTGGCCCTRTCSCTCCCGGCCAAATSAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAG
GTGGGACACGTGCGACCGGGAYAGSGAGGGCCGGTTTASTCTCTCGGGTCCCCTTCGCTATAGCGACCGTGTTGCGAGTC
HPVHAGPXXPGQXREPRGSDIAGTTLR>
                                                                 11680
                                                        11670
                                                11660
                              nef 76-105 (184)
                     11630
             11620
    11610.
GCCCATGACATATAAGGSCGCTRTTGACCTCAGCYTGTTTCTGAAAGAGAAAGGCGGACTGGAWGGCCTCRTCTATAGCM
CGGGTACTGTATATTCCSGCGAYAACTGGAGTCGRACAAAGACTTTCTCTTTCCGCCTCACCTWCCGGAGYAGATATCGK
 PHTYKXAX DLS LFLKEKGGLXGLXY S>
                                                        11750
                              11720
                                        vpr 1-30 (112)
                      11710
   spacers
AGAAAGCTGCTATGGAACAGGCTCCCGAAGACCAARGCYCTCAGAGAGAGCCTTACAATGAGTGGRCCCTGGAGCTCCTG
TCTT CGACGATACCTTGTCCGAGGGCTTCTGGTTYCGRGAGTCTCTCTCGGAATGTTACTCACCYGGGACCTCGAGGAC
X K A A M E Q A P E D Q X X Q R E P Y N E W X L E L L>
                                               poi 481-510 (66)
                                       11810
                              11800
                      11790 .
             11780
    11770
GAAGAGCTCAAGHAHGAGGCTCAAGRCCAATGGACCTWCCAAATCTWTCAGGAACCCTTTAAGAATCTGAAAACCGGAAA
CTTCTCGAGTTCKTKCTCCGAGTTCYGGTTACCTGGAWGGTTTAGAWAGTCCTTCGGAAATTCTTAGACTTTTGGCCTTT
E E L K X B A Q X Q W T X Q I X Q E P P K N L K T G K>
                                                                 11920
                                                        11910
                                                11900
                                       11890
                              11880
                      11870
             11860
    11850
GTATKCCAGAAWGAGARGCGCTCACACAAAQTGGATGACAGAWACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGW
CATAMGGTCTTWCTCTYCGCGAGTGTGTTTCACCTACTGCTTWTGGGAGGACCAGGTCTTACGGTTAGGGCTAACGTTCW
Y X R X R X A H T N W M T X T L L V Q N A N P D C K>
                                                11980
                                       11970
                               11960
                      11950
 gag 316-345 (22)
12070
                                                12060
                                       12050
                              12040
            gag 166-195 (12)
    12010
12150
                                                12140
                     gag 241-270 (17)
                                       12130
             12100
12090
  TXNPPXPVGXIYKRWILGLT
                                                                 12240
                                                12220
                              pol 241-270 (50)
                      12190
             12180
     12170
CCGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACRAARRQCAA
GGCCGGAGTTCTTTTCTTTTCGCAGTGGCAGGACCTACACCCTCTGCGAATGAAGTCGCAGGGGGAGCTGYTTYYGGTT
AGLKKKKSVTVLDVGDAYFSVPLDXX
                                                                  12320
                                                        12310
                                       pol 541-570 (70)
                               12280
                      12270
             12260
     12250
{\tt ARGGAAACCTGGGAGRCTTGGTGGAYGGAMTACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATACCCCTCC}
TYCCTTTGGACCCTCYGAACCACCTRCCTKATGACCGTCCGATGGACCTAAGGACTCACCCTCAAACACTTATGGGGAGG
 X E T W E X W W X X Y W Q A T W I P E W E F V N T P P>
                                               nef 121-150 (187)
                                        12370
                      12350
                               12360
             12340
     12330
CCTCGTCTTTCCCGATTGGCAWAACTATACCCCTGGCCCTGGCRYAAGGTATCCCCTCACCTTTGGATGGTGCTTTAAGC
GGAGCAÇAAAGGGCTAACCGTWTTGATATGGGGACCGGGACCGYRTTCCATAGGGGAGTGGAAACCTACCACGAAATTCG
       FPDWXNYTPGPGXRYPLTFGWCFK>
                                                                  12480
                                                pol 571-600 (72)
                                        12450
                               12440
                      12430
              12420
TCGTGCCTGTGGACCCQAAACTGTGGTACCAACTGGAAAAGGAMCCCATTGYCGGAGYCGAAACCTTTTACGTGGACGGA
AGCACGGACACCTGGGGTTTGACACCATGGTTGACCTTTTCCTKGGGTAACRGCCTCRGCTTTGGAAAATGCACCTGCCT
L. V P V D P K L W Y Q L E K X P I X G X E T F Y V D G>
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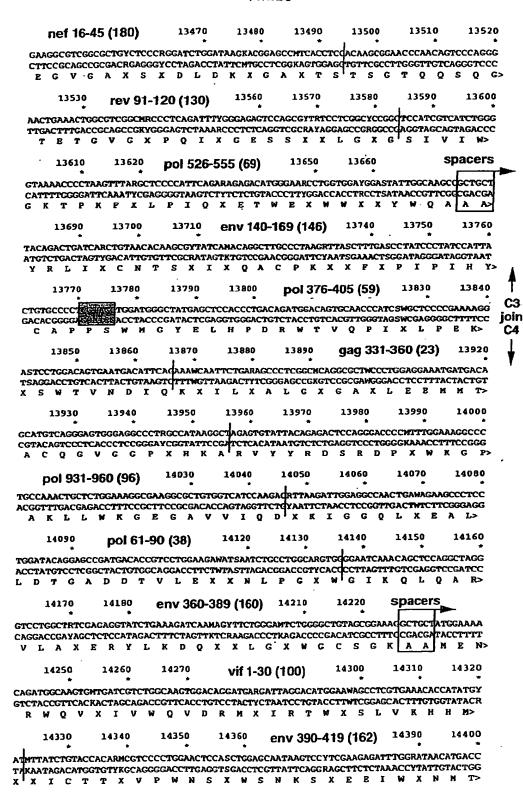
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12490 12500 12510 12520 gag 136-165 (10) GCCGCCARCAGAGACAAAGCTCGGGCAAAACSYCCAGGGACAGATGGTGCATCAGSCTWTTAGCCCCAGGACCCTCAA CGGCGGTYGTCTCTCTGTTTCGAGCCGGTTTTGSRGGTCCCTGTCTACCACGTAGTCSGAKAATCGGGGTCCTGGGAGTT AAXRETKLGQNXQGQMVHQXXSPRTLN> 12570 12580 12590 12600 <sup>12610</sup> env 61-90 (141) 12640  ${\tt CGCTTGGGTCAAGGTCRTCGAAGAGAAAGSCTTTAR} \\ {\tt GAHACCGAAGTGCATAACGTCTGGGCTACCCATGCCTGTGTGC}$ GCGAACCCAGTTCCAGYAGCTTCTCTTTCSGAAATYGCTRTGGCTTCACGTATTGCAGACCCGATGGGTACGGACACACG
A W V K V X E E K X F X X T E V H N V W A T H A C V> 12650 12670 12680 12690 12700 12710 12720 CTACCGATCCCAATCCCCAAGAGRITSWCCTGGAGAATGTGACAGAGCTCAAGGATCACHAAYTCCTCGGCHTTTGGGGA GATGGCTAGGGTTAGGGGTTCTCYAASWGGACCTCTTACACTGTCTGGAGTTCCTAGTCKTTRAGGAGCCGKAAACCCCT T D P N P Q E X X L E N V T E L K D Q X X L G X W G> 12750 12760 env 375-404 (161) 12770 12780 12790 12800 TGCTCCGGCAAAHTCATTTGCACAACCRNTGTGCCTTGGAACAGCWCCTGGTCCAACHAKCTGGCCATAACAAGTGGG ACGAGGCCGTTTKAGTAAACGTGTTGGYKACACGGAACCTTGTCGWGGACCAGGTTGGKTMGACCGGTATTGTTTCACCC C S G K X I C T T X V P W N S X W S N X X G H N K V G> vif 136-165 (109) 12840 12850 12860 12870 12880 AAGCCTCCAGTATCTGGCTCTGAMGGCTCTGATTAMGCCTAAGAAAATCARACCCCCTCTGCCTAGGGYTAAGACAATCA TTCGGAGGTCATAGACCGAGACTKCCGAGACTAATKCGGATTCTTTTAGTYTGGGGGAGACGGATCCCRATTCTGTTAGT S L Q Y L A L X A L I X P X K I X P P L P S X spacers 12890 12900 env 230-254 (152) 12930 12960 TTGTGCATCTGAATRAGTCCGTGGWAATCAATTGCACAAGGCCTARCAATAACACAAGGAMGCCGCG raacwa. AACACGTAGACTTAYTCAGGCACCWTTAGTTAACGTGTTCCGGATYGTTATTGTGTTCCTKCCGGCGG CATCUCTTCWT JOIN V H L N X S V X I N C T R P X N N T R X A A A S E X> 12970 12990 gag 106-135 (8) 13020 13030 13040 CAGANWAAGTCCMAACAGAAAACCCAGCAAGCCGCCGCCGATACAGGCRCTCCAGCMAGGTCAGCCAAAACTATCCCAT GTCTTWTTCAGGKTTGTCTTTTGGGTCGTTCGGCCGCCGCTATGTCCGTYGAGGTCGKTCCAGTCGGTTTTGATAGGGTA Q X K S X Q R T Q Q A A A D T G X S S X V S Q N Y P I> 13050 13060 13070 13080 pol 826-855 (89) TGTCTCCAACTTTACCTCCRCCRCTGTGAAAGCCGCTTGTTGGTGGGCCRRTATCMAACAGGAGTTTGGAATCCCTTACA AGGTTGAAATGGAGGYGGYGACACTTTCGGCGAACAACCACCCGGYYATAGKTTGTCCTCAAACCTTAGGGAATGT 13140 13130 13150 13160 13170 pol 586-615 (73) ATCCCCAAAGCCAAACATTCTATGTGGATGGCGCTGCCARTAGGGAAACCAAACTGGGAAAGGCTGGCTATGTGACAGAC TAGGGGTTTCGGTTTGTAAGATACACCTACCGCGACGGTYATCCCTTTGGTTTGACCCTTTCCGACCGATACACTGTCTG N P Q S Q<sup>I</sup>T P Y V D G A A X R E T K L G K A G Y V T D> 13210 13220 13230 13240 13250 pol 766-795 (85) agaggcagacagaaartcrttagdggaatctggcagctcgactgtacccatctggaaggcaaartcattctggtagccgt TCTCCGTCTCTTTYAGYAATC4CCTTAGACCGTCGAGCTGACATGGGTAGACCTTCCGTTTYAGTAAGACCATCGGCA R G R Q K X X S G I W Q L D C T H L B G K X I L V A V> 13310 13320 13330 13340 13350 CCACGTCGCCTCCGCTACATTGAGGCTGAGGTGGCAATGAGCAAGTGGATAAGCTCGTGAKTKCCGGAATCAGAAAGG GGTGCAGCGGAGGCCGATGTAACTCCGACTCCAGCCGTTACTCGTTCACCCTATTCGAGCACTMAMGGCCTTAGTCTTTCC
H V A S G Y I E A E V G N E Q V D K L V X X G I R K> pol 691-720 (80) 13390 13400 13410 13420 13430 TGCTATTCCTCGACGGAATCRATAAGGCTCAGGAAGGACACGAAGGATAAGGATTAGGCRARCCSCTCCCGCTGCT ACGATAAGGACCTCCCTTAGYTATTCCGAGTCCTTCTCGTGCTTCAGTCCCTTTCCTAATCCGYTYGGSGAGGCGACGA V L F L D G I X K A Q E E H E V R E R I R X X X P A A>

C3

FIGURE 15 (Cont) **SUBSTITUTE SHEET (RULE 26)** 

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### FIGURE 15 (Cont)

C4 join C5

14410 14430 14420 vpu 16-45 (133) 14460 14470 14480 TGGATKSAATGQCTGATTWTCGCTATCGTCGTGTGGACCATTGYGTWTATCGAATACARGAAACTGCTCARGCAAAGGAR ACCTAMSTTACCGACTAAKAGCGATAGCAGCACCCTGGTAACRCAWATAGCTTATGTYCTTTGACGAGTYCGTTTCCTY W X X W L I X A I V V W T I X X I E Y X K L L X Q R X> 14490 14510 14520 gag 46-75 (4) 14550 AATCGATAGGCTCATCRAAAGGCTCAACCCTGGCCTCCTGGAAACCKCTGAGGGATGTHAACAGATCCTGGRACAGCTCC TTAGCTATCCGAGTAGYTTTCGGACTGGGACCGGAGGACCTTTGGAGACCCTACAKTTGTCTAGGACCYTGTCGAGG

I D R L I X R L N P G L L P T X E G C X Q I L X Q L> 14570 14580 14590 14600 14610 vpu 31-60 (134) 14670 14680 14690 14700 14710 AGANYCAGAGAGAGAGCCGAAGACTCCGGCAATGAGTCCGAGGGAGAACACCCGGAATCAGATACCAATACAATGTGCT TETTRETCTCTCTCCCCCTTCTGAGGCCGTTACTCAGGCTCCCTCTQTGTGGGCCTTAGTCTATGGTTATGTTACACGA R X R E R A E D S G N E S E G D T P G I R Y Q Y N V L> 14730 pol 286-315 (53) 14760 14770 14780 14790 14800 CCCCCAAGGCTGGAAGGGCTCCCCASCCATTTTCCAAAGCTCCATCHCCMAAATCCTCATGATGCAAAGGGGAAACTTTA GGGGGTTCCGACCTTCCCGAGGGGTSGGTAAAAGGTTTCCAGGTACKGGRTTTAGGAGTACTACGTTTCCCCTTTCAAAT
PQGNKGSPXIFQSSNXXILNMQRGNF gag 376-405 (26) 14850 14860 14870 RGGGACMGAAAAGGATTRTCAAGTGCTTCAACTGTGGAAAGGAAGGCCATMTCGCTARGAATTGCAGACCTCCCCTGGAG YCCCTGRCTTTTCCTAAYAGTTCACGAAGTTGACACCTTTCCTTCCGGTARAGCGATYCTTAACGTCTGGAGGGACCTC
X G X K R I X K C P N C G K E G H X A X N C R P P L E> 14900 14890 14910 14940 rev 76-105 (129) AGACTGMACCTGGATTGCTCCGAGGATWGCGRCACCTCCGGCACAGGCAAAGCCAAAGGCACAGAGAACAGGAGTGGGA<mark>/</mark>CT TCTGACKTGGACCTAACGAGGCTCCTAWCGCYGTGGAGGCCGTGTGTGTGTTTCGGTTCCGTGTCTTCTCTCACCCTGA R L X L D C S E D X X T S G T Q Q S Q G T E T G V G | 14970 14980 14990 15000 poi 781-810 (86) CGTGGCTGTGCATGTGGCCAGGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTM GCACCGACACGTACACCGGTCGCCTATATAGCTTCGGCTTCACTAGGGACGGCTTTGACCTGTCCTTTGGCGAATGAAAK AVHVASGYIEAEVIPAETGQETAY 15050 15060 15070 15080 15090 env 200-229 (150) TCCTCAAGATTARGCCTGTGGTCAGCACAGCTCCTCCTCAACGGTAGCCTCGCTGAAGAGGAARTCRTTATCAGAAGC AGGAGTTQTAATYCGGACACCAGTCGTGTGTCGAGGACGACTTGCCATCGGAGCGACTTCTCCTTYAGYAATAGTCTTCG X L K<sup>I</sup>I X P V V S T Q L L N G S L A B B B X X I R S> 15130 15140 15150 15160 pol 406-435 (61)  ${\tt GAAAACYTTACCRATAAdAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACSCTGGCATCAAAGTGARGCAACTCTTTTGRAATGGYTATTTTTTGACCAGCCGTTTGACTTAACCCGAAGGGTTTAGATGSGACCGTAGTTTCACTYCGTTGA$ E N X T X N K L V G K L N W A S Q I Y X G I K V X Q L> 15210 15220 15230 15240 15250 env 121-139 (145) GTGTAAGCTCCTGAGAGGCRCCAAAGCCCTCACCCCTCTGTGTGACACTGAATTGCACAAACGCTAACCTCATCAATG CACATTCGAGGACTCTCCGYGGTTTCGGGAGTGGGGGAGACACACACTGTGACTTACGTGTTTCCGATTGGAGTACTTAC
C K L L R G X K A L T P L C V T L N C T N A N L I N> spacers 15310 15360 15320 15330 tat 76-102 (123) TGAATGCTCCTCAAMCCAGAGGCGATAACCCTACCGRTCCCRAAGAGTCCAAGAARAGGTCGMGTCCAAGRCAGAGACA actt4cgacg/gitkggtctccgctattgggatggcyagggyttctcaggttcttytccagckcaggttcygtctctgt N A A Q X R G D N P T X P X E S K K X V X S K X E T>

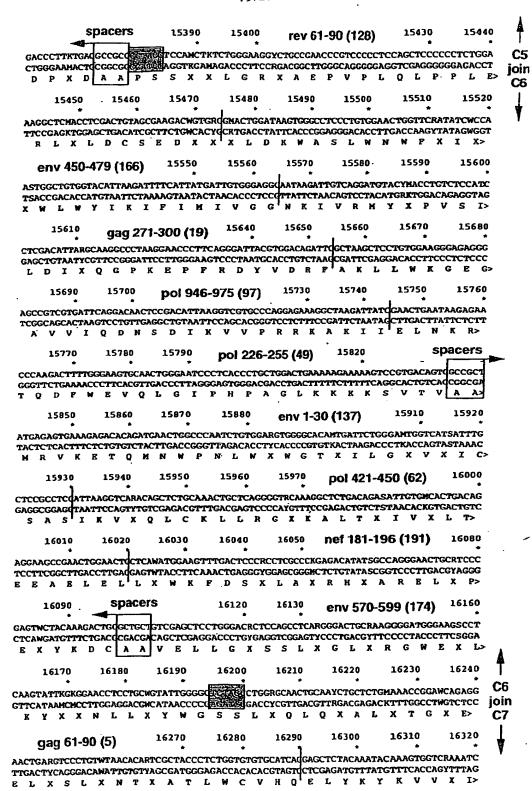


FIGURE 15 (Cont)

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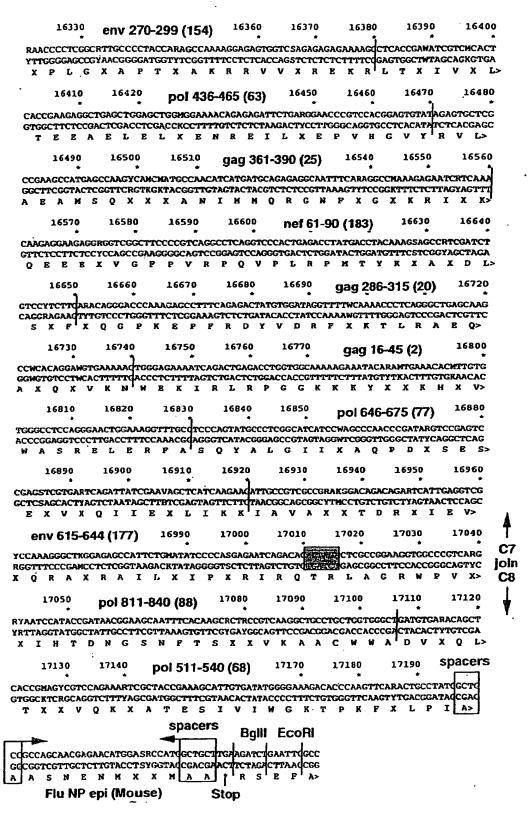
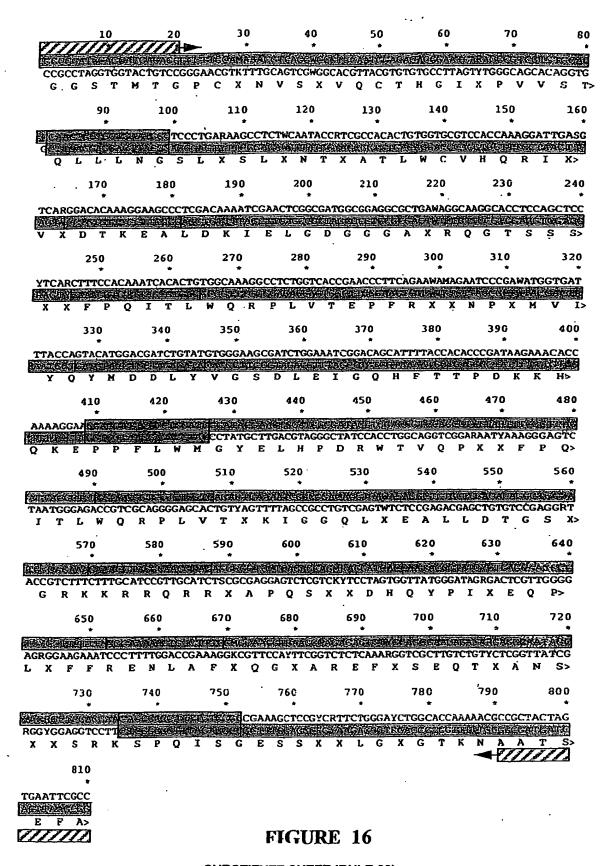


FIGURE 15 (Cont)



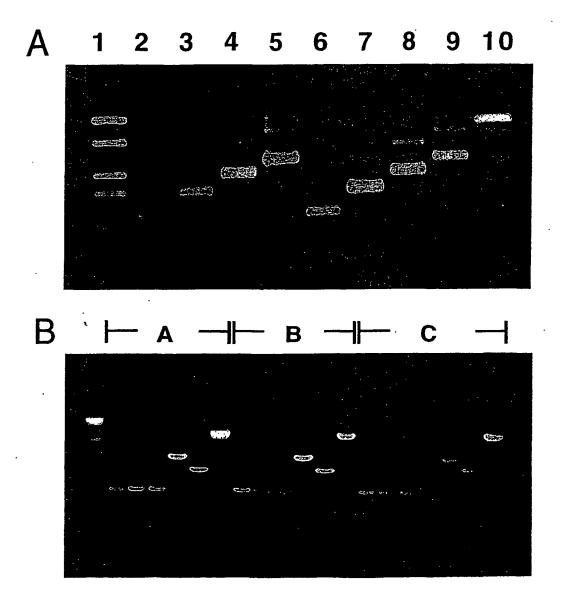


FIGURE 17

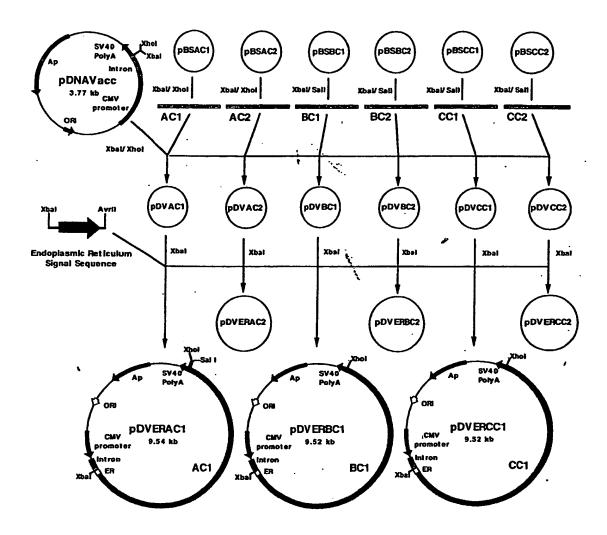


FIGURE 18A

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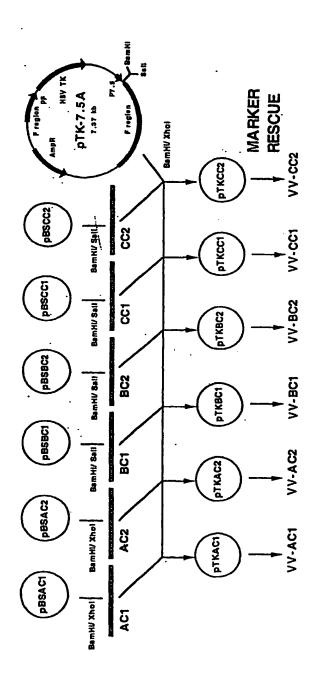


FIGURE 18B

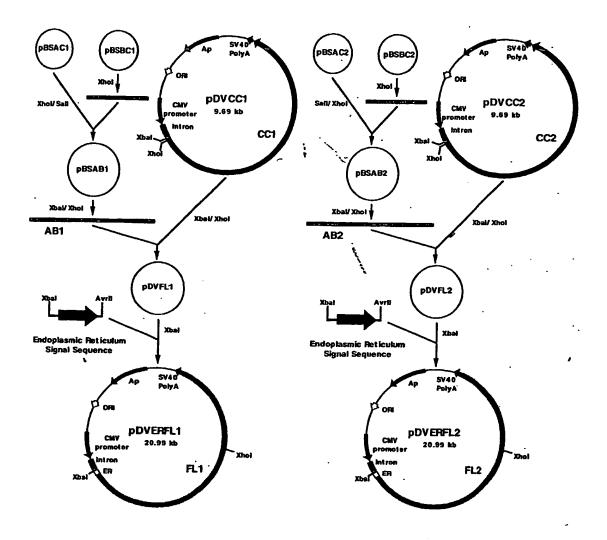
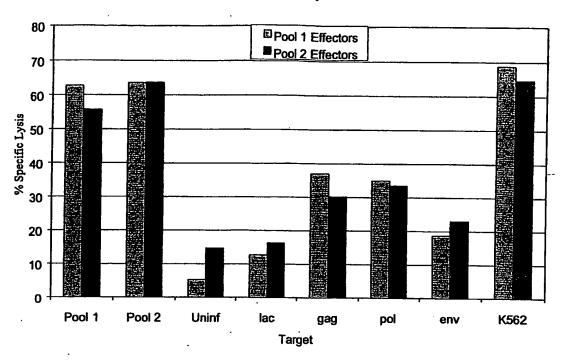


FIGURE 18C

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## Subject1





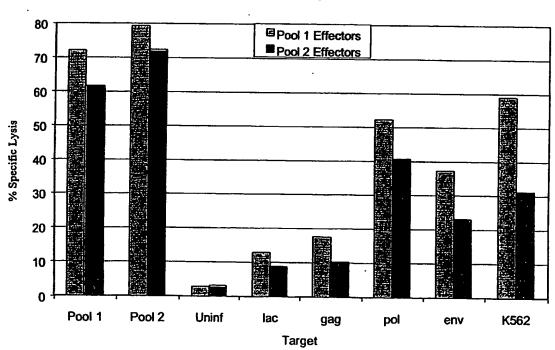


FIGURE 19

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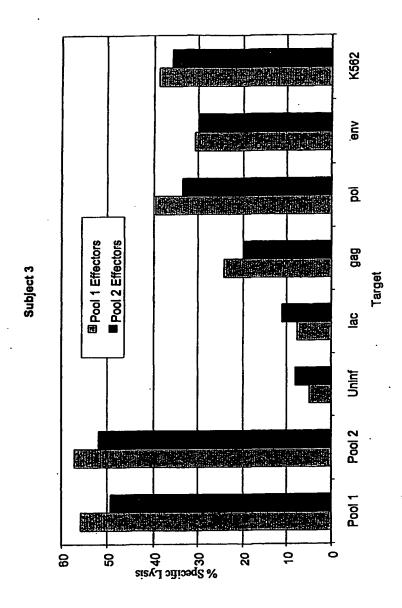


FIGURE 19 (Cont)

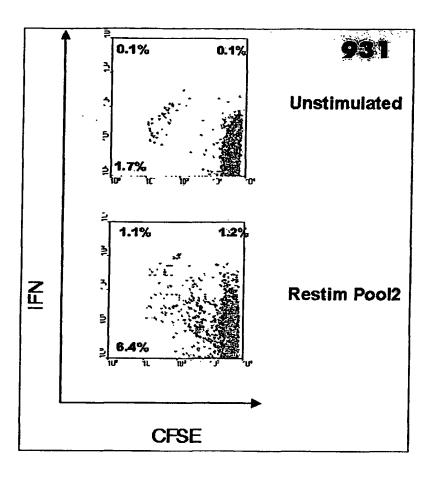


Figure 20

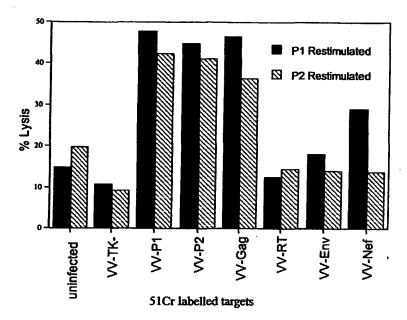


Figure 21

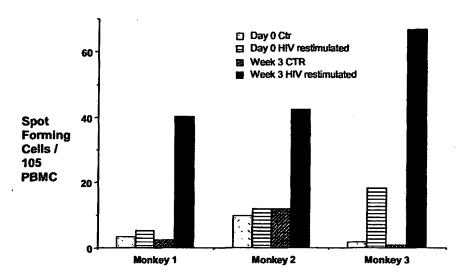


Figure 22A

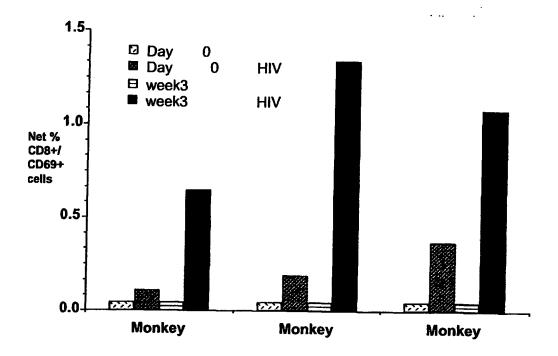


Figure 22B

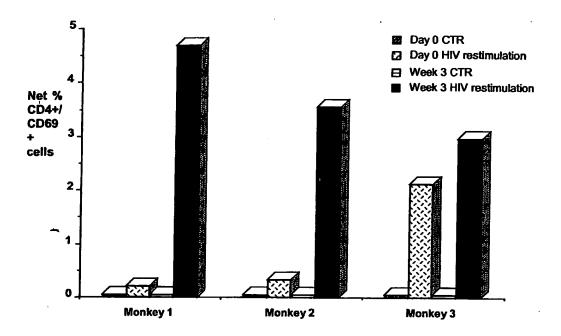


Figure 22C

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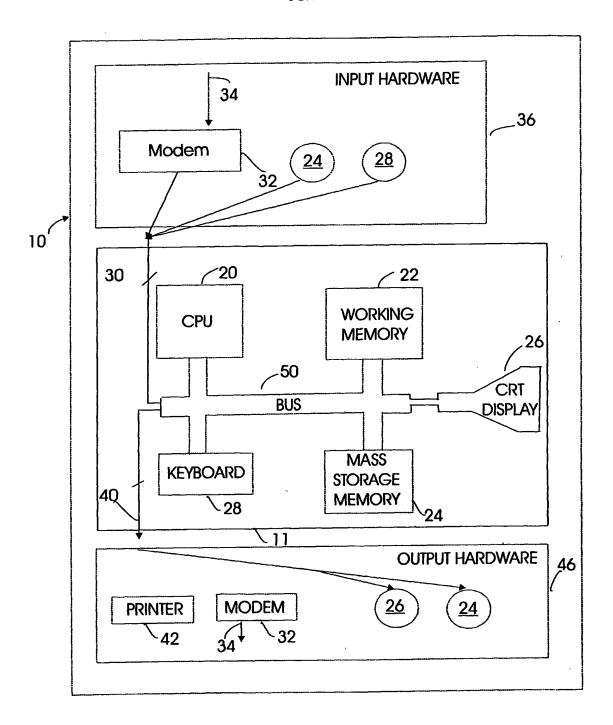


FIGURE 23

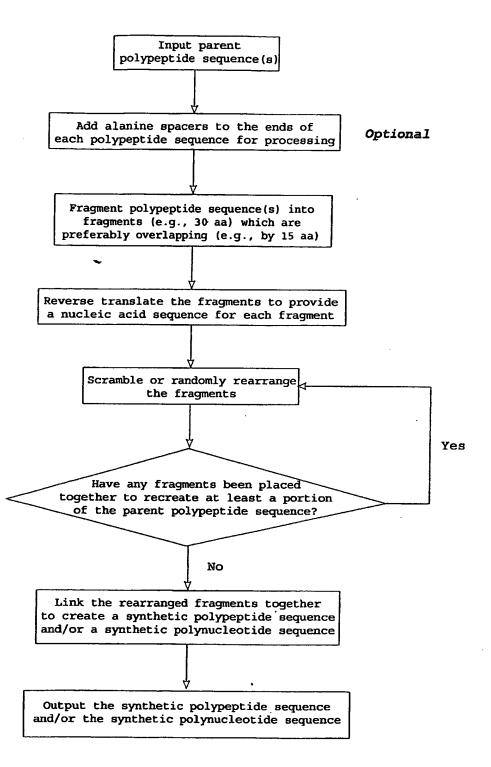


Figure 24

```
/* Scramble */
                                                     95/216
  /* Includes */
  #include <stdio.h>
  #include <stdlib.h>
  #include <string.h>
  #include <time.h>
 /* Constant definitions */
 /* Version Information */
 #define VERSION_NO
                                                                       "0.2"
 #define VERSION_DATE
                                                           "04/03/1999"
 /* Misc */
 #define KEYBOARD_BUFFER_SIZE
                                               256
                                                                      /*size of keyboard read buffer */
 #define LEN_CODON
                                                                                  /*length of codon (including
 null) */
 #define BUFFER SIZE
                                                                      10000
                                                                                  /*size of file read buffer */
 #define TRUE
                                                                                             /*boolean true */
 #define FALSE
                                                                      0
                                                                                             /*boolean false */
 /* Error codes */
#define E_NOERROR
#define E_NOINFILE
#define E_MALLOC
                                                          0
                                                                                 /*no error */
                                                           1
                                                                                 /*genes file not found */
                                                          2
                                                                                 /*memory allocation error */
 #define E_FILEREAD
                                                          3
                                                                                 /*file read error */
 #define E_CREATE_OUTPUT_FILE
                                                                      /*error creating output file */
#define E_OVERLAP
                                                          5
                                                                                 /*segment overlap >= length
/* Structure definitions */
typedef struct gene GENE;
typedef GENE * P_GENE;
typedef struct gene_segment GENE_SEGMENT;
typedef GENE_SEGMENT * P GENE SEGMENT:
struct gene {
           char * name;
           char * data;
           P_GENE next_gene;
};
struct gene_segment {
           P_GENE p_gene;
           int number;
           int offset;
           int first_codon_choice;
           char * amino data:
           char * dna data;
           P_GENE_SEGMENT next_seg;
}:
```

```
96/216
   /* Function prototypes */
   int prolog();
   int get parameters();
   int read_int(char * prompt);
   int load genes();
   int add gene(char * gene name,char * gene data);
   void insert_gene(P_GENE * head,P_GENE new_gene);
  int add_aa();
  int split_genes();
  int split_gene(P_GENE g);
  int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg);
  int convert segments aa to dna();
  int convert aa to dna(char * aa ptr,char * dna ptr,int first choice):
  char * codon(char acid_char,int preferred);
  int perform_scramble();
  int scramble segments();
  int adjacent segments();
  int display genes();
  int write_output_file();
  void strip_newline(char * strip_str);
  void pad_amino_string(char * amino_ptr, char * padded_ptr);
  int even(int test num);
 void read_str(char * prompt,char * string);
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file);
 int user_confirmation();
 void test();
 /* Global variables */
 char * codon_table[26][2] = {
 /" A 00 "/ {"GCC","GCT"},
/" - 01 "/ {"???","???"},
/" C 02 "/ {"TGC","TGT"},
/" D 03 "/ {"GAC","GAT"},
 /" E 04 */ {"GAG","GAA"},
 /" F 05 "/ {"TTC", "TTT"},
 /* G 06 */ {"GGC","GGA"},
 /" H 07 */ {"CAC","CAT"},
/" 108 */ ("ATC", "ATT"),
/" - 09 */ ("???", "???"),
/" K 10 */ {"AAG", "AAA"},
/" L 11 */ {"CTG", "CTC"),
/" M 12 */ {"ATG", "ATG"),
/" N 13 */ {"AAC", "AAT"),
/" - 14 */ ("???" "????")
 /* - 14 */ {**???","???"},
 /" P 15 */ {"CCC", "CCT"}.
/" Q 16 "/ {"CAG","CAA"},
 /" R 17 "/ {"AGG","AGA"},
/" S 18 "/ {"AGC","TCC"},
/" T 19 "/ {"ACC","ACA"},
/" - 20 "/ {"???","???"},
/" V 21 "/ {"GTG","GTC"},
/" W 22 "/ {"TGG","TGG"},
```

Figure 25 (Cont)

```
/" - 23 */ {"???","???"},
/" Y 24 */ {"TAC","TAT"},
                                                     97/216
 /* - 25 */ {"???","???"}
};
char * error_text[] = {
/* 00 */ ···
/* 01 */ ,"ERROR: Input file not found!"
/* 02 */ ,"ERROR: Memory allocation error"
/* 03 */ ,"ERROR: File read error"
/* 04 */ ,"ERROR: Could not create output file"
/* 05 */ ,"ERROR: Segment overlap must be less than segment length"
char disease name[KEYBOARD BUFFER SIZE]:
char input_file_name[KEYBOARD_BUFFER_SIZE];
char output_file_name[KEYBOARD_BUFFER_SIZE];
int num genes = 0;
int num segments = 0;
int len segment;
int segment_overlap;
P_GENE first_gene = NULL;
P_GENE_SEGMENT first_segment = NULL;
P_GENE_SEGMENT * scrambled_segments = NULL;
/* Mainline */
void main() {
           int error = E_NOERROR;
           printf("Scramble - Version %s, %s\n\n", VERSION_NO, VERSION_DATE);
           /* Initial processing */
           if (!error)
                      error = prolog();
           /* Get various program parameters from user */
           if (!error)
                      error = get_parameters();
           /* Load genes from genes file */
           if (!error)
                      error = load genes();
           /* Add 'AA' to start and end of all genes */
           if (!error)
                      error = add_aa();
          /* Split genes into overlapping chunks */
          if (!error)
                      error = split_genes();
          /* Convert segment amino acid to dna */
          if (!error)
                      error = convert_segments_aa_to_dna();
```

Figure 25 (Cont)

```
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             /* Scramble the segments */
              if (!error)
                          error = perform_scramble();
             /* Write output file */
             if (!error)
                          error = write_output_file();
             /* Show error if there was one */
             if (error)
                          printf("%s\n",error_text[error]);
 }
 /* prolog() */
 /* Perform any initial processing required */
 int prolog() {
             /* Seed the random number generator, using the system clock */
             /* Don't run the program more than once in the same second! */
             /* Or we'll get the same randomisation!!!!!!!!!!!!!! */
             srand(time(NULL));
             return E_NOERROR;
}
/* get_parameters() */
/* Ask for various parameters from the user (stdin) */
     Disease name
     Input file name
     Output file name
     Segment length
int get_parameters() {
            int valid;
            read_str("Enter disease name : ",disease_name);
read_str("Enter input file name : ",input_file_name);
read_str("Enter output file name : ",output_file_name);
            valid = FALSE;
            while (!valid) {
                         len_segment = read_int("Enter segment length : ");
                         if (len segment % 2)
                                     printf("Segment length must be even!\n");
                         else
                                     valid = TRUE;
            segment overlap = len_segment / 2;
            return E NOERROR;
/* load_genes() */
```

Figure 25 (Cont)

```
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/* Load the genes from the input file */
int load_genes() {
    FILE * input_file;
           char name _buf[BUFFER_SIZE];
           char data_buf[BUFFER_SIZE];
           /* Open genes file for reading */
           if (NULL == (input file = fopen(input_file_name, "r")))
                      return E_NOINFILE;
           printf("Loading genes from: %s\n",input_file_name);
           num_genes = 0;
           /* Read gene name */
           while (NULL != read_nonblank_line(name_buf,BUFFER_SIZE,input_file)) {
                      /* Read the gene data */
                     if (NULL != read_nonblank_line(data_buf,BUFFER_SIZE,input_file)) {
                                 /* Allocate memory for new gene and add to list */
                                 if (rc = add_gene(name buf,data buf))
                     }
          /* Close genes file */
          fclose(input_file);
          return rc;
}
/* add gene() */
/* Allocate memory for new gene, then insert in list */
int add_gene(char * gene_name,char * gene_data) {
          P_GENE new_gene;
          /* Allocate storage for new gene */
          if (NULL == (new_gene = malloc(sizeof(GENE))))
                     return E MALLOC;
          /* Initialise new gene */
          new gene->next gene = NULL;
          /* Allocate storage for gene name (+1 for null) */
          if (NULL == (new_gene->name = malloc(strlen(gene_name)+1)))
                     return E_MALLOC;
          /* Store gene name */
          strcpy(new gene->name,gene name);
          /* Allocate storage for gene data (+1 for null) */
          if (NULL == (new_gene->data = malloc(strlen(gene_data)+1)))
                     return E_MALLOC;
          /* Store gene data */
          strcpy(new_gene->data,gene_data);
          /* Insert the new gene into linked list */
          insert_gene(&first_gene,new_gene);
          /* Increment num_genes */
          num_genes++;
```

Figure 25 (Cont)

```
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            return E_NOERROR;
 }
 /* insert_gene() */
 /* Insert gene into linked list */
 void insert_gene(P_GENE * head_gene,P_GENE new_gene) {
            P_GENE * cur_ptr = head_gene;
           while (NULL != (*cur_ptr))
                      cur_ptr = &((*cur_ptr)->next_gene);
            *cur_ptr = new_gene;
}
/* add_aa() */
/* Add 'AA' to the start and end of every gene */
int add_aa() {
           P_GENE cur_gene = first_gene;
           char * new_data;
           while (NULL != cur_gene) {
                      /* Allocate storage to fit the gene plus four characters */
                      new_data = malloc(strien(cur_gene->data)+5);
                      /* Shift gene data to new storage, add "AA" */
                      strcpy(new data, "AA");
                      strcat(new_data,cur_gene->data);
                      strcat(new_data,"AA");
                      /* Free previous gene data storage */
                      free(cur gene->data);
                      /* Set gene data pointer to new storage */
                      cur_gene->data = new_data;
                      /* Advance to next gene */
                      cur_gene = cur_gene->next_gene;
          }
          return E_NOERROR;
}
/* split_genes() */
/* Split the genes into overlapping segments */
int split_genes() {
          P_GENE cur_gene = first_gene;
          P_GENE_SEGMENT cur_seg = first_segment;
          printf("Splitting genes into segments...\n");
          /* Split the genes into segments */
          while (NULL != cur_gene) {
                     /* Split the gene */
                     split_gene(cur_gene);
                     /* Advance to next gene */
```

Figure 25 (Cont)

```
cur_gene = cur_gene->next gene;
           }
           /* Count the number of segments */
           num_segments = 0;
           cur_seg = first_segment;
           while (NULL != cur_seg) {
                     num segments++;
                     cur_seg = cur_seg->next_seg;
           }
           return E_NOERROR;
/* split gene() */
/* Split a gene into overlapping segments */
P_GENE_SEGMENT new_segment = NULL;
          int done;
          int seg ctr = 0;
          /* Allocate memory for segment buffer */
          if (NULL == (seg_buf = malloc(len_segment+1)))
                    return E_MALLOC;
          /* Insert a null at the end of the segment buffer, */
          /* so we can use it as a string */
          seg_buf[len_segment] = '\0';
          /* Set segment pointer to start of gene data */
          seg_ptr = g->data;
          done = FALSE;
          while (!(done)) {
                    /* So we know if we copied data */
                    seg_buf[0] = '\0';
                   /* Copy a segment of gene data to the segment buffer */
                   memcpy(seg_buf,seg_ptr,len_segment);
                   /* If there was some gene data copied to the buffer */
                   if (NULL != seg_buf[0]) {
                              /* Allocate storage for a new segment */
                              if (NULL == (new_segment = malloc(sizeof(GENE_SEGMENT))))
                                         return E MALLOC:
                              /* Increment segment counter */
                              seg_ctr++;
                              /* Setup the new segment */
                              new_segment->p_gene = g;
                              new_segment->number = seg ctr;
                              new_segment->offset = seg_ptr - g->data + 1;
                              new segment->next seg = NULL:
```

Figure 25 (Cont)

```
if (NULL == (new_segment->amino_data = malloc(len_segment+1)))
                                           return E MALLOC;
                                if (NULL == (new_segment->dna_data = malloc(len_segment*3+1)))
                                           retum E_MALLOC;
                                new_segment->amino_data[0] = '\0';
                                new_segment->dna_data[0] = 10;
                                /* Copy segment data from buffer to new segment */
                                strcpy(new_segment->amino_data,seg_buf);
                                /* Insert new segment into chain from gene */
                                insert_segment(&first_segment,new_segment);
                     `}
                      /* If we didn't read a full segment, we are finished! */
                     if (strlen(seg_buf) < len_segment)
                                done = TRUE;
                     /* Otherwise, advance segment pointer to next segment in buffer */
                                seg_ptr = seg_ptr + len_segment - segment overlap;
          }
}
/* insert segment() */
/* Insert a segment node at the end of the list */
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg) {
          P_GENE_SEGMENT * cur ptr = head seg;
          while (NULL != (*cur_ptr))
                     cur_ptr = &((*cur_ptr)->next_seg);
          *cur_ptr = new_seg;
/* convert_segments_aa_to_dna */
/* Go thru segments, and for each, convert amino acids to dna */
int first_choice = 1;
          int alternate;
          printf("Converting to DNA...\n");
          /* Work out if we need to alternate the first codon choice or not */
          /* Don't need to do this anymore, since the segment length is
          /* forced to be even, and the overlap is half the length (odd). */
          /*alternate = ((even(len_segment) && even(segment_overlap))
                               || (leven(len_segment) && leven(segment_overlap)));*/
          alternate = FALSE:
          while (NULL != cur_seg) {
                    cur_seg->first_codon_choice = first_choice;
                    convert_aa_to_dna(cur_seg->amino_data,cur_seg->dna_data,
                                                                        cur_seg->first codon choice);
```

```
/* Address next segment */
                         cur_seg = cur_seg->next_seg;
                         /* If we are alternating, alternate the first codon choice */
                         /*if (alternate)
                                     if (1 == first_choice)
                                                first_choice = 2;
                                     else
                                                first choice = 1:1/
             }
             return E_NOERROR;
  }
  /* convert_aa_to_dna */
 /* Converts a string of amino acid to dna */
 /* NOTE: assumes that buffer at dna_ptr is large enough to hold dna!!! */
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice) {
             char * p_codon;
             int cur_preferred = first choice;
            while ('\0' != *aa_ptr) {
                        p_codon = codon(*aa_ptr,cur_preferred);
                        strcat(dna_ptr,p_codon);
                        /* If we didn't find a codon, log a warning */
                        if (0 == strcmp(p\_codon,"???\overline{0}"))
                                   printf("WARNING: no codon found for arnino acid!\n");
                        /* Alternate current preferred codon */
                        if (1 == cur_preferred)
                                   cur_preferred = 2;
                       else
                                   cur_preferred = 1;
                       aa_ptr++;
           return E_NOERROR;
/* codon */
/* Returns a pointer to a codon corresponding to the amino acid passed */
/* The codon pointer is to 3 characters, plus a terminating null */
char * codon(char acid_char,int preferred) {
           int codon_table_index;
           char * codon ptr;
           /* Determine index into codon_table (table starts at 'A') */
           codon_table_index = acid_char - 'A';
           /* Set pointer to appropriate codon */
           codon_ptr = codon_table[codon_table_index][preferred-1];
```

```
return codon_ptr;
 }
 /* display_genes() */
 /* Display the name and data for all genes */
 int_display_genes() {
            P_GENE cur_gene = first_gene;
            while (NULL != cur gene) {
                       printf("%s\n",cur_gene->name);
printf("%s\n",cur_gene->data);
                       cur_gene = cur_gene->next_gene;
            }
            return E_NOERROR;
 }
/* perform_scramble() */
 /* Scramble the segments */
/* Check for adjacent segments. If there are, rescramble */
 int perform_scramble() {
           int done = FALSE;
           int rc = E_NOERROR;
           while (TRUE) {
                      rc = scramble_segments();
                      if (E_NOERROR == rc)
                                  if (adjacent_segments()) {
                                             printf("Adjacent segments detected! Rescramble? (y/n) ");
                                             if (!user_confirmation()) {
                                                        printf("WARNING: Adjacent segments in output
file.\n");
                                                        break;
                                            }
                                 else
                                            break;
                      else
                                 break;
          }
           return rc;
}
/* scramble segments() */
/* Randomly scramble the segments, putting pointers in scrambled segments[] */
int scramble_segments() {
          P_GENE_SEGMENT cur_seg = first_segment;
          P_GENE_SEGMENT temp;
          printf("Scrambling segments...\n");
```

Figure 25 (Cont)

```
/* Allocate storage for array of segment pointers */
            if (NULL == (scrambled_segments = malloc(sizeof(P GENE SEGMENT)*num segments)))
                       return E MALLOC;
            /* First, initialise scrambled_segments in same order as linked list */
            while (cur_seg != NULL) {
                       scrambled_segments[i] = cur_seg;
                       cur_seg = cur_seg->next_seg;
            }
            /* Now, randomly scramble the segments */
            for (i=0;i<num segments;i++) {
                                    = rand() % num segments;
                                      = scrambled_segments[i];
                       scrambled_segments[i] = scrambled_segments[j];
                       scrambled_segments[j] = temp;
           }
           return E_NOERROR;
}
/* adjacent_segments() */
/* Determine if the scrambled segment order has resulted in */
/* two segments which were adjacent originally (ie every */
/* second one) have ended up adjacent.
int adjacent_segments() {
           int i:
           int rc = 0;
           P_GENE_SEGMENT cur_seg;
           P_GENE_SEGMENT next_seg;
           for (i=0;i<num segments-1;i++) {
                      /* Address current and next segments */
                      cur_seg = scrambled_segments[i];
                      next_seg = scrambled_segments[i+1];
                      /* Do segments come from same gene, and are two apart? */
                      if (((cur_seg->p_gene == next_seg->p_gene)
                                && ((cur_seg->number == (next_seg->number)+2)
                                           (cur_seg->number == (next_seg->number)-2))))
                                return 1:
           return 0;
/* write_output_file() */
/* Write out segments (in initial non-scrambled order) */
/* Write out synthetic protein (in scrambled order) */
/* Write out synthetic dna (in scrambled order) */
int write_output_file() {
          FILE * output file;
```

```
char * amino buffer;
 P GENE SEGMENT cur seg;
 int i;
 /* Open output file for writing (erase any contents) */
 if (NULL == (output_file = fopen(output_file_name, "w")))
             return E_CREATE_OUTPUT_FILE;
 /* Allocate memory for padded amino string buffer */
 if (NULL == (amino_buffer = malloc(len_segment*3+1)))
             return E_MALLOC;
 printf("Writing output file: %s\n".output file name);
 /* Write output file header information */
 fprintf(output_file,"Scramble %s - Output File\n", VERSION_NO);
fprintf(output_file, "\n");
fprintf(output_file, "Disease name : %s\n", disease_name);
 fprintf(output_file;"Input filename : %s\n",input file name);
fprintf(output_file,"Output filename: %s\n",output_file_name);
fprintf(output_file,"Number genes : %d\n",num_genes);
fprintf(output file,"Number segments: %d\n",num segments);
fprintf(output file, "Segment length: %d\n", len segment);
fprintf(output_file, "Segment overlap: %d\n", segment_overlap);
/* Write out segments in initial non-scrambled order */
fprintf(output_file,"\n");
fprintf(output_file, "Segments in original order:\n");
fprintf(output file,"-
cur seg = first segment;
while (NULL != cur_seg) {
            /* Format amino data to line up with codons */
            pad_amino_string(cur_seg->amino_data,amino_buffer);
            fprintf(output_file,"Gene : %s\n",cur_seg->p_gene->na
fprintf(output_file,"Segment# : %d\n",cur_seg->number);
fprintf(output_file,"Offset : %d\n",cur_seg->offset);
                                        : %s\n",cur_seg->p_gene->name);
            fprintf(output_file,"1st Codon : %d\n",cur_seg->first_codon_choice);
            fprintf(output_file, "%s\n", amino_buffer);
            fprintf(output_file, "%s\n", cur_seg->dna_data);
            fprintf(output file,"\n");
            cur seg = cur seg->next_seg;
/* Write out segment names in scrambled order */
fprintf(output_file, "Segments in scrambled order:\n");
fprintf(output file,"--
for (i=0;i<num_segments;i++) {
            /* Format amino data to line up with codons */
            pad_amino_string(scrambled_segments[i]->amino_data,amino_buffer);
            /* Write segment details */
            fprintf(output_file,"%s #%d\n",scrambled_segments[i]->p_gene->name,
                       scrambled segments[i]->number):
            fprintf(output file,"%s\n",amino buffer);
            fprintf(output file, "%s\n", scrambled segments[i]->dna data);
           fprintf(output_file,"\n");
```

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```
}
             /* Write synthetic protein in one long string */
             fprintf(output_file, "Synthetic Protein:\n");
             fprintf(output file,"--
             for (i=0;i<num_segments;i++)
                        fprintf(output_file,"%s",scrambled_segments[i]->amino_data);
             fprintf(output_file,"\n\n");
            /* Write synthetic dna in one long string */
             fprintf(output_file, "Synthetic DNA:\n");
             fprintf(output_file,"-----
                                          —\n");
             for (i=0;i<num_segments;i++)
                        fprintf(output_file, "%s", scrambled_segments[i]->dna_data);
            retum E_NOERROR;
 }
 /* strip_newline() */
 /* Replace the first newline character with a null */
 void strip_newline(char * strip_str) {
            char * newline pos;
            /* Find the newline char */
            newline pos = strchr(strip str,\n');
            /* If we found one, replace it with a null */
            if (NULL != newline_pos)
                       newline pos[0] = 10;
}
/* pad_amino_string */
/* Copy amino chars from amino_ptr to padded_ptr, padding each */
/* side with a space. */
void pad_amino_string(char * amino ptr, char * padded ptr) {
           while ('\0' != *amino_ptr) {
                       *padded_ptr = ' ':
                       padded_ptr++;
                        *padded_ptr = *amino_ptr;
                       padded_ptr++;
                       *padded_ptr = ' ';
                       padded_ptr++;
                       amino ptr++;
           }
           /* Stick a null at the end of the padded string */
           *padded ptr = '\0';
}
/* even() */
/* True if test_num is even, otherwise false */
```

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```
int even(int test_num) {
             return !(test_num % 2);
 /* read int() */
 /* Read an integer from stdin. Keep trying until valid int > 0 entered. */
 /* Return the integer read, or 0 if error reading from stdin. */
 int read_int(char * prompt) {
             char buffer[KEYBOARD_BUFFER_SIZE];
            int value read;
            int valid = FALSE;
            while (!valid) {
                        printf("%s",prompt);
                        valid = TRUE;
                        fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
                        if (1 != sscanf(buffer, "%d", &value_read))
                                 valid = FALSE;
                        if (valid && (value_read < 1))
                                   valid = FALSE:
                        if (!valid)
                                   printf("Positive integer value please!\n");
            }
            return value read;
}
/* read_str() */
/* Read a string from the user (stdin) */
/* Strip the newline from it */
void read_str(char * prompt,char * string) {
            char buffer[KEYBOARD_BUFFER_SIZE];
            printf(prompt);
            fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
           sscanf(buffer, "%s", string);
}
/* read_nonblank_line() */
/* Read a line from file until we get a non-blank one */
char * read_nonblank_line(char * buf,int buf size,FILE * in file) {
           char * return_ptr;
           /* Read lines until we get a non-black one, or EOF */
                       return_ptr = fgets(buf,buf_size,in_file);
           while ((NULL != return_ptr) && (('\n' == buf[0]) || (' ' == buf[0])));
           /* If we got a line, change the newline char to a null */
           if (NULL != return_ptr)
                      strip newline(buf);
```

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HepC Savine design

## HepC la consensus polyprotein sequence used for scramble program

MSTNPKPQRKTKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATRKTSERSQPRGRRQPIPKARRPEGRTWAQ PGYPWPLYGNEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNLGKVIDTLTCGFADLMGYIPLVGAPLGGAARALAHGVR VLEDGVNYATGNLPGCSFSIFLLALLSCLTVPASAYQVRNSTGLYHVTNDCPNSSIVYRAADAILHTPGCVPCVREGN ASRCWVAMTPTVATRDGKLPATQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLPTFSPRRHWTTQGCNCSIYPGH ITGHRMAWDMMNWSPTAALVMAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVVLLLFAGVDAETHVTGG NAGRTTSGLVSLLTPGAKQNIQLINTNGSWHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTDFDOG WGPISYANGSGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAPTYSWGANDTDVFVLNNTRPPL GNWFGCTWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTDCFRKHPEATYSRCGSGPWITPRCLVDYPYRLWHYPCTINY TIFKVRMYVGGVEHRLEAACNWTRGERCDLEDRDRSELSPLLLSTTQWQVLPCSFTTLPALSTGLIHLHQNIVDVQYL YGVGSSIASWAIKWEYVVLLFLLLADARVCSCLWMMLLISQAEAALENLVILNAASLAGTHGLVSFLVFFCFAWYLKG RWVPGAVYALYGMWPLLLLLLALPQRAYALDTEVAASCGGVVLVGLMALTLSPYYKRYISWCLWWLQYFLTRVEAQLH VWVPPLNVRGGRDAVILLMCVVHPTLVFDITKLLLAVFGPLWILQASLLKVPYFVRVQGLLRICALARKMIGGHYVQM AIIKLGALTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVVFSQMETKLITWGADTAACGDIINGLPVSARRGREILLGP ADGMVSKGWRLLAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGAGTRTIAS PKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRRGDSRGSLLSPRPISYLKGSSGGPLL CPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTMRSPVFTDNSSPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAAOG YKVLVLNPSVAATLGFGAYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSI LGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEBVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELA  ${f AKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAV$ SRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEG  ${\tt VFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLT$  ${\tt HPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPAIIPDREVLYREFDEMEECSQHLP}$ YIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAGLSTLPGNPAIASLMAFT AAVTSPLTTSQTLLFNILGGWVAAQLAAPGAATAFVGAGLAGAAIGSVGLGKVLVDILAGYGAGVAGALVAFKIMSGE VPSTEDLVNLLPAILSPGALVVGVVCAAILRRHVGPGEGAVQWMNRLIAFASRGNHVSPTHYVPESDAAARVTAILSS LTVTQLLRRLHQWISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYKGVWRGDGIMHTR CHCGAEITGHVKNGTMRIVGPRTCRNMWSGTFPINAYTTGPCTPLPAPNYTFALWRVSAEEYVEIRRVGDFHYVTGMT  ${\tt TDNLKCPCQVPSPEFFTELDGVRLHRFAPPCKPLLREEVSFRVGLHEYPVGSQLPCEPEPDVAVLTSMLTDPSHITAE}$ AAGRRLARGSPPSMASSSASQLSAPSLKATCTANHDSPDAELIEANLLWRQEMGGNITRVESENKVVILDSFDPLVAE EDEREISVPABILRKSRRFAQALPVWARPDYNPPLVETWKKPDYEPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTL STALAKLATKSFGSSSTSGITGDNTTTSSEPAPSGCPPDSDAESYSSMPPLEGEPGDPDLSDGSWSTVSSEAGTEDVV CCSMSYSWTGALVTPCAAEEQKLPINALSNSLLRHHNLVYSTTSRSACQRQKKVTFDRLQVLDSHYQDVLKEVKAAAS KVKANLLSVEBACSLTPPHSAKSKFGYGAKDVRCHARKAVAHINSVWKDLLEDSVTPIDTTIMAKNEVFCVOPBKGGR KPARLIVFPDLGVRVCEKMALYDVVSKLPLAVMGSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSYDTRCFDSTVTESD IRTERAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCGYRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQDCTMLVCGDDLVVICESAGVQEDAASLRAFTEAMTRYSAPPGDPPQPEYDLELITSCSSNVSVAHDGAGKRVYYLTRDP TTPLARAAWETARHTPVNSWLGNIIMFAPTLWARMILMTHFFSVLIARDQLEQALDCEIYGACYSIEPLDLPPIIQRL HGLSAFSLHSYSPGEINRVAACLRKLGVPPLRAWRHRARSVRARLLARGGRAAICGKYLFNWAVRTKLKLTPIAAAGR LDLSGWFTAGYSGGDIYHSVSHARPRWFWFCLLLLAAGVGIYLLPNR

```
Scramble - Output File
Scramble version: 0.1 beta, 08/02/1999
              : 1
Num. genes
               : 201
Num. segments
Segment length
              : 30
Segment overlap : 15
Segments in original order:
Gene '
        : HepCla
Segment# : 1
Offset
         : 1
1st Codon : 1
A A M S T N P K P Q R K T K R N T N R R P O D V K P P G G G
GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA
```

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Gene : HepCla
Segment# : 2
Offset : 16
1st Codon : 1

N T N R R P Q D V K P P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

Gene : HepCla Segment# : 3 Offset : 31 1st Codon : 1

Gene : HepCla Segment# : 4 Offset : 46 1st Codon : 1

Gene : HepCla
Segment# : 5
Offset : 61
lst Codon : 1

R G R R Q P I P K A R R P E G R T W A Q P G Y P W P L Y G N AGGGGAAGGACAGCCTAACCCTAAGGCTAAGGCAAACCCGAAGCAACCCGGATACCCTTGGCCTCTATGGCAAT

Gene : HepCla Segment# : 6 Offset : 76 1st Codon : 1

R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S AGGACATGGGCTGGCCTGTGCCCCAGAGGCTCCCGAGAGGCTGGCCTGGCCCGGAGGCTCC

Gene : HepCla Segment# : 7 Offset : 91 1st Codon : 1

EGCGWAGWLLSPRGSRPSWGPTDPRRRSRNGGGGGATGCGGTGGCTGGCTGCCTAGGGGAAGCCCTCCTGGGGACCCACAGACCCTAGGAGAGCCCAAGAAGTCCAGGAAT

Gene : HepCla Segment# : 8 Offset : 106 lst Codon : 1

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACCACATGCGGATTCGCTGACCTC

Gene : HepCla Segment# : 9 Offset : 121 1st Codon : 1

L G K V I D T L T C G P A D L M G Y I P L V G A P L G G A A CTGGGAAAGGTCATCGATACCCTCACCTGTGGCTTTGCCGATCTGATGGCTATACCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT

Gene : HepCla Segment# : 10 Offset : 136 1st Codon : 1

M G Y I P L V G A P L G G A A R A L A H G V R V L B D G V N ATGGGATACATTCCCCTCGTGGGAGGCCCTCTGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT

Gene : HepCla Segment# : 11 Offset : 151 1st Codon : 1

1st Codon: 1
R A L A H G V R V L B D G V N Y A T G N L P G C S F S I F L
AGGGCTCTGGCTCACGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATGCCACGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTC

Gene : HepCla Segment# : 12 Offset : 166

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1st Codon : 1 Y A T G N L P G C S F S I F L L A L L S C L T V P A S A Y Q TAGGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA : HepCla Gene Segment# : 13 Offset : 181 1st Codon : 1 L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT Gene : HepCla Segment# : 14 Offset : 196 1st Codon : 1 V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T GTGAGAAACTCCACCGGACTGTATCACGTCACCAATGACTGTCCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACA Gene : HepCla Segment# : 15 Offset : 211 1st Codon : 1 N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT Gene : HepCla Segment# : 16 Offset. : 226 1st Codon : 1 P G C V P C V R B G N A S R C W V A M T P T V A T R D G K L CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCCACAGTGGCTACCAGAGACGGAAAGCTC Gene : HepCla Segment# : 17 Offset : 241 1st Codon : 1 W V A M T P T V A T R D G K L P A T Q L R R H I D L L V G S Gene : HepCla Segment# : 18 Offset : 256 1st Codon : 1 PATQLRRHIDLLVGSATLCSALYVGD CGS CCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTTGGGCTCC Gene : HepCla Segment# : 19 Offset : 271 1st Codon : 1 A T L C S A L Y V G D L C G S V F L V G Q L P T F S P R R H GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT Gene : HepCla Segment# : 20 Offset : 286 1st Codon : 1 V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTTATCCCGGACACATT Gene : HepCla Segment# : 21 Offset : 301 W T T Q G C N C S I Y P G H I T G H R M A W D M M M N W S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGGACATGATGAACTGGAGCCCT Gene : HepCla Segment# : 22 Offset : 316 1st Codon : 1 T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCCTCCTGAGAATCCCTCAGGCT

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: HepCla Segment# : 23 Offset : 331 1st Codon : 1 TAALVMAQLLRIPQAILDMIAGAHWGVLAG ACCECTGCCCTCGTGATGCCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA : HepCla Segment# : 24 Offset : 346 1st Codon : 1 I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V : HepCla Segment# : 25 Offset : 361 1st Codon : 1 I A Y P S M V G N W A K V L V V L L L F A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACTGGCCCAAAGTGCTCGTGGTCCTGCTCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA Gene : HepCla Segment# : 26 Offset : 376 1st Codon : 1 V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTCGCGGCGCGAGGCACACCCCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGCTCC : HepCla Segment# : 27 1st Codon : 1 G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGCAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA Gene : HepCla Segment# : 28 : 406 Offset 1st Codon : 1 T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC Gene : HepCla Segment# : 29 Offset : 421 1st Codon : 1 S W H I N S T A L N C N B S L N T G W L A G L P Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACACAAATTCAAT : HepCla Gene Segment# : 30 Offset : 436 N T G W L A G L P Y Q H K F N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA : HepCla Segment# : 31 Offset : 451 1st Codon : 1 S S G C P B R L A S C R R L T D P D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC : HepCla Segment# : 32 Offset : 466 1st Codon : 1 D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT

Gene : HepCla Segment# : 33

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Offset 1st Codon : 1 G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C GGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCCTAAAAGCGTCTGCGGACCCGTCTACTGT : HepCla Gene Segment# : 34 Offset : 496 1st Codon : 1 C G I V P A K S V C G P V Y C P T P S P V V G T T D R S G : HepCla Segment# : 35 Offset : 511 1st Codon : 1 PTPSPVVGTTDRSGAPTYSWGANDTDVPV TTCACACCCTCCCCGTCGTCGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC Gene : HepCla Segment# : 36 : 526 1st Codon : 1 A P T Y S W G A N D T D V P V L N N T R P P L G N W P G C T GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA Gene : HepCla Segment# : 37 Offset : 541 1st Codon : 1 LNNTRPPLGNWPGCTWMNSTGPTKVCGAPP CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT Gene : HepCla Segment# : 38 : 556 Offset 1st Codon : 1 W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T Gene : HepCla Segment# : 39 Offset : 571 1st Codon: 1 C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G TEGETCATCEGAGGCECTGCCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA Gene : HepCla Segment# : 40 1st Codon : 1 D C F R K H P B A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT Gene : HepCla Segment# : 41 Offset SGPWITPRCLVDYPYRLWHYPCTINYTIPK AGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTTCAAA Gene : HepCla : 42 Segment# : 616 1st Codon : 1 RLWHYPCTINYTIFKVRMYVGGVEHRLEAA AGGCTCTGGCATTACCCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTGGAACACAGACTGGAAGCCGCT Gene : HepCla Segment# : 43 Offset : 631 1st Codon : 1 V R M Y V G G V B H R L B A A C N W T R G B R C D L B D R D

## 115/216

GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGGAAAGGTGTGACCTCGAGGATAGGGAT : HepCla Gene Segment# : 44 Offset : 646 1st Codon : 1 C N W T R G B R C D L B D R D R S B L S P L L L S T T Q W Q TGCAATTGGACAAGGGGAGAGAGATGCGATCTGGAAGACAGAGACAGAGCGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA Gene : HepCla Segment# : 45 Offset : 661 1st Codon : 1 R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G AGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGCTCTGCCCCCGGA Gene : HepCla Segment# : 46 : 676 Offset 1st Codon : 1 V L P C S F T T L P A L S T G L I H L H Q N I V D V O Y L Y : HepCla Gene Segment# : 47 Offset : 691 1st Codon : 1 L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W B Y CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT : HepCla Gene Segment# : 48 Offset : 706 1st Codon : 1 G V G S S I A S W A I K W E Y V V L L F L L L A D A R V C S GGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC Gene : HepCla Segment# : 49 Offset : 721 V V L L F L L A D A R V C S C L W M M L L I S Q A E A A L Gene : HepCla Segment# : 50 Offset : 736 1st Codon : 1 C L W M M L L I S Q A B A A L B N L V I L N A A S L A G T H TECCTCTEGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT : HepCla Segment# : 51 Offset : 751 1st Codon : 1 B N L V I L N A A S L A G T H G L V S F L V F F C F A W Y L GAGAATCTGGTCATCCTCAACGCTGCCTCGCTGGCACACACGGACTGGTCAGCTTTCTGGTCTTTTGCTTTGCCTGGTCACCTC Gene : HepCla Segment# : 52 : 766 Offset 1st Codon: 1
G L V S P L V F P C P A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG Gene : HepCla Segment# : 53 Offset 1st Codon : 1 K G R W V P G A V Y A L Y G M W P L L L L L L A L P Q R A Y AAGGGAAGGTGGCCTGGCGCTGTTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGGCCTCAGAGAGCCCTAT

Gene : HepCla

PCT/AU01/00622 WO 01/090197

## 116/216

Segment# : 54 Offset : 796 1st Codon : 1 W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L : HepCla Segment# : 55 Offset : 811 1st Codon : 1 A L D T B V A A S C G G V V L V G L M A L T L S P Y Y K R Y GCCCTCGACACAGAGGTCGCCCCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT : HepCla Segment# : 56 Offset : 826 1st Codon : 1 V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V GTGGGACTGATGCCCTCACCCTCACCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGCCTGCAATACTTTCTGACAAGGGTC : HepCla Segment# : 57 Offset : 841 1st Codon : 1 I S W C L W W L Q Y F L T R V B A Q L H V W V P P L N V R G ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA : HepCla Segment# : 58 : 856 1st Codon : 1 BAQLHVWVPPLNVRGGRDAVILLMCVVHPT GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA Gene : HepCla Segment# : 59 Offset : 871 G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGAGACGCTGTGATTCTGCTCATGTGTGTGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTGTTTTGGCCCT Gene : HepCla Segment# : 60 Offset : 886 1st Codon : 1 LVFDITKLLLAVFGPLWILQASLLKVPYFV CTGGTCTTCGATATCACAAAGCTCCTGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTC Gene : HepCla Segment# : 61 Offset : 901 1st Codon : 1 LWILQASLLKVPYPVRVQGLLRICALARKM CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAGATG : HepCla Segment# : 62 : 916 1st Codon : 1 R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT Gene : HepCla Segment# : 63 Offset : 931 1st Codon : 1 I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT : HepCla

Segment# : 64 Offset : 946 1st Codon: 1

## 117/216

```
L T G T Y V Y N H L T P L R D W A H N G L R D L A V A V E P
 CTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGAGCCT
 Gene
         : HepCla
 Segment# : 65
 Offset
        : 961
 1st Codon : 1
 WAHNGLRDLAVAVEPVVFSQMETKLITWGA
 TGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCAGGACCCGTCGTCTTTAGCCAAATGGAAACCAAACTGATTACCTGGGGCGCGCT
 Gene
         : HepCla
 Segment# : 66
 Offset
         : 976
 1st Codon : 1
 V V P S Q M B T K L I T W G A D T A A C G D I I N G L P V S
 GTGGTCTTCTCCCAGATGGAGACAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTCGCGATATCATTAACGGACTGCCTGTGTCC
Gene
         : HepCla
Segment# : 67
Offset
        : 991
1st Codon : 1
 D T A A C G D I I N G L P V S A R R G R E I L L G P A D G M
Gene
        : HepCla
Segment#
       : 68
Offset
        : 1006
1st Codon : 1
 ARRGREILLGPADGMVSKGWRLLAPITAYA
GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCT
        : HepCla
Segment#
       : 69
Offset
        : 1021
1st Codon : 1
 V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T
GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA
Gene
        : HepCla
Segment# : 70
Offset
        : 1036
1st Codon : 1
 Q Q T R G L L G C I I T S L T G R D K N Q V B G B V Q I V S
CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC
Gene
        : HepCla
Segment#
       : 71
Offset
       : 1051
1st Codon : 1
G R D K N Q V E G E V Q I V S T A A Q T P L A T C I N G V C
GGCAGAGACAAAAACCAAGTGGAAGGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT
Gene
       : HepCla
Segment# : 72
Offset
       : 1066
1st Codon : 1
TAAQTFLATCING V C W T V Y H G A G T R T I A S P
ACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCT
        : HepCla
Segment#
       : 73
       : 1081
Offset
1st Codon : 1
W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L
TGGACAGTGTATCACGGAGCCGGAACCAGACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC
Gene
       : HepCla
Segment# : 74
Offset
       : 1096
1st Codon : 1
K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C
AAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCAAGGCTCCAGGTCCCTGACACCCTGT
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118/216 Gene : HepCla Segment# : 75 Offset : 1111 1st Codon : 1 V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D GTGGGATGGCCTCCCGGGAAGCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTCACCTCGTGACAAGGCATGCCGAT Gene : HepCla Segment# : 76 Offset : 1126 1st Codon : 1 T C G S S D L Y L V T R H A D V I P V R R G D S R G S L L ACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGAGGGCGATAGCAGAGGCTCCCTGCTC Segment# : 77 Offset : 1141 1st Codon : 1 V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P Gene : HepCla Segment# : 78 Offset : 1156 S P R P I S Y L K G S S G G P L L C P A G H A V G I P R A A AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT Gene : HepCla Segment# : 79 Offset : 1171 1st Codon : 1 L L C P A G H A V G I F R A A V C T R G V A K A V D F I P V Gene : HepCla Segment# : 80 Offset : 1186 1st Codon : 1 V C T R G V A K A V D F I P V E N L E T T M R S P V F T D N GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT : HepCla Segment# : 81 Offset : 1201 1st Codon : 1 ENLETT M R S P V F T D N S S P P A V P Q S F Q V A H L GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCGGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC : HepCla Gene Segment# : 82 Offset S S P P A V P Q S F Q V A H L H A P T G S G K S T K V P A A Gene : HepCla Segment# : 83 Offset : 1231 1st Codon : 1 H A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V Gene : HepCla Segment# : 84 Offset : 1246

TACGCTGCCCAAGGCTATAAGGTCCTGGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGA

Gene : HepCla
Segment# : 85

: 1261

1st Codon : 1

YAAQGYKVLVLNPSVAATLGFGAYMSKAHG

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1st Codon : 1 A A T L G P G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA Gene : HepCla Segment# : 86 Offset : 1276 1st Codon : 1 I D P N I R T G V R T I T T G S P I T Y S T Y G K F L A D G ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA Gene : HepCla Segment# : 87 : 1291 1st Codon : 1 S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT Gene : HepCla Segment# : 88 Offset : 1306 1st Codon : 1 G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGGGGGGGGCCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC Gene : HepCla Segment# : 89 Offset : 1321 1st Codon : 1 H S T D A T S I L G I G T V L D Q A B T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGTCGCCACA Gene : HepCla Segment# : 90 Offset : 1336 1st Codon : 1 DQABTAGARLVVLATATPPGSVTVPHPNIR GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCAATCCCAATATCGAA : HepCla Segment# : 91 Offset : 1351 1st Codon : 1 A T P P G S V T V P H P N I B B V A L S T T G B I P F Y G K GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA Gene : HepCla Segment# : 92 Offset : 1366 1st Codon : 1 BVALSTTGEIPFYGKAIPLEVIKGGR<sub>HLI</sub> GAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT Gene : HepCla Segment# : 93 Offset : 1381 1st Codon : 1 A I P L B V I K G G R H L I F C H S K K K C D E L A A K L V GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTC Gene : HepCla Segment# : 94 Offset : 1396 C H S K K K C D B L A A K L V A L G I N A V A Y Y R G L D V TGCCATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC Gene : HepCla Segment# : 95 Offset : 1411 1st Codon : 1 A L G I N A V A Y Y R G L D V S V I P T S G D V V V A T D GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT

## 120/216

: HepCla Segment# : 96 Offset : 1426 1st Codon : 1 SVIPTSGDVVVVATDALMTGYTGDPDSVID AGGGTCATCCCTACCTCCGGCGATGTGGTCGTCGTCGCCACAGACGCTCTGATGACCCGGATACACACGCCGATTTCGATAGCGTCATCGAT : HepCla Segment# : 97 Offset : 1441 1st Codon : 1 A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT Gene : HepCla Segment# : 98 Offset : 1456 1st Codon: 1
CNTCVTQTVDFSLDPTFTIETTTLPQDAVS TGCANTACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC Gene : HepCla Segment# : 99 : 1471 1st Codon : 1 T F T I B T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGCCTGGCATT Gene : HepCla Segment# : 100 Offset : 1486 RT Q R R G R T G R G K P G I Y R P V A P G B R P S G M F D : HepCla Segment# : 101 Offset : 1501 1st Codon: 1
YRFVAPGBRPSGMFDSSVLCBCYDAGCAWY TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT : HepCla Segment# : 102 Offset : 1516 1st Codon : 1 SSVLCBCYDAGCAWYELTPAETTVRLRAYM AGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATG Gene : HepCla Segment# : 103 : 1531 BLTPARTTVRLRAYMNTPGLPVCQDHLEPW GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGG Gene : HepCla Segment# : 104 1st Codon : 1 NTPGLPVCQDHLBFWEGVFTGLTHIDAHFL AACACACCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC Gene : HepCla

Segment# : 105 Offset : 1561 1st Codon : 1

B G V F T G L T H I D A H F L S Q T K Q S G E N F P Y L V A GAGGGAGTGTTTACCGGACTGACACACATTGACGCTCACTTTCTGTCCCAGACAAAGCGAGAGAAGTTTCCCTTACCTCGTGGCT

Gene : HepCla Segment# : 106

121/216 Offset : 1576 1st Codon : 1 S Q T K Q S G E N F P Y L V A Y Q A T V C A R A Q A P P P S Gene : HepCla Segment# : 107 Offset : 1591 1st Codon : 1 YQATVCARAQAPPPSWDQMWKCLIRLKPTL TACCAAGCCACAGTGTGTGCCAGAGCCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC Gene : HepCla Segment# : 108 Offset : 1606 1st Codon : 1 W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V O N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT Gene : HepCla Segment# : 109 Offset : 1621 H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT Gene : HepCla Segment# : 110 Offset : 1636 1st Codon : 1 EVTLTHPVTKYIMTCMSADLEVVTSTWVLV Gene : HepCla Segment# : 111 Offset : 1651 1st Codon : 1 M S A D L E V V T S T W V L V G G V L A A L A A Y C L S T G Gene : HepCla Segment# : 112 Offset : 1666 1st Codon : 1 G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGAGTGCTCGCCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT Gene : HepCla Segment# : 113 : 1681 Offset C V V I V G R I V L S G K P A I I P D R B V L Y R E F D E M TECETCETEATTETEGEAAGGATTETECTCAGCEGAAAGCCTGCCATTATCCCTGACAGAGGGTCCTGTATAGGGAATTCGATGAGATG Gene : HepCla Segment# : 114 Offset : 1696 1st Codon : 1 IIPDRBVLYREFDEMBECSQHLPYIEQGMM ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG : HepCla Gene Segment# : 115 Offset : 1711 1st Codon : 1 E B C S Q H L P Y I B Q G M M L A B Q F K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA Gene : HepCla Segment# : 116 Offset : 1726 1st Codon : 1

Figure 26 (Cont)

L A B Q F K Q K A L G L L Q T A S R Q A B V I A P A V Q T N

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CTGGCTGAGCAATTCAAACAGAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT
```

Gene : HepCla Segment# : 117 Offset : 1741 1st Codon : 1

ASRQAEVIAPAVQT NWQKLEVFWAKHMWNFGCCTCCAGGCAAGCCGAAGCGAAGCGAAGCGAAGCGCAAGCCGACCTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTTGGGCTAAGCATATGTGGAACTTT

Gene : HepCla Segment# : 118 Offset : 1756 1st Codon : 1

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

Gene : HepCla Segment# : 119 Offset : 1771 1st Codon : 1

Gene : HepCla Segment# : 120 Offset : 1786 1st Codon : 1

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G AACCCTGCCATTGCCTCCTGATGGCCTTTACCGTTGCCTCCCCCTCACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGA

Gene : HepCla Segment# : 121 Offset : 1801 1st Codon : 1

S P L T T S Q T L L F N I L G G W V A A Q L A A P G A A T A AGCCCTCTGACAACCTCCCAGACACCTCTCAATATCCTCGGGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

Gene : HepCla Segment# : 122 Offset : 1816 1st Codon : 1

Gene : HepCla Segment# : 123 Offset : 1831 1st Codon : 1

PVGAGLAGAAIGSVGLGKVLVDILAGYGAGTCGGGCTCGGCGAAGTGCTCGTCGGCTGGATACCTCGCCGGATACGGAGCCCGGA

Gene : HepCla Segment# : 124 Offset : 1846 1st Codon : 1

L G K V L V D I L A G Y G A G V A G A L V A F K I M S G B V CTGGGAAAGGTCCTGGCGTCGACATTCTGGCTGGCTATGGCGCTGGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTC

Gene : HepCla Segment# : 125 Offset : 1861 1st Codon : 1

VAGALVAFKIMSGEVPSTEDLVNLLPAILS
GTGGCTGGCGCTCTGCCCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCCTGCCATCTGTCC

Gene : HepCla Segment# : 126 Offset : 1876 1st Codon : 1

Gene : HepCla

## 123/216

Segment# : 127 Offset : 1891 1st Codon : 1

PGALVVGVCAAILRRHVGPGBGAVQWMNRCCCCGGAGCCCTGGCGAAGGCGCTGTGCATGATGATGAACAGA

Gene : HepCla Segment# : 128 Offset : 1906 1st Codon : 1

R H V G P G E G A V Q W M N R L I A F A S R G N H V S P T H
AGGCATGTGGGACCCGGAGAGGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTTAGCAGAGGCAATCACGTCAGCCCTACCCAT

Gene : HepCla Segment# : 129 Offset : 1921 1st Codon : 1

LIAFASRGNHVSPTHYVPBSDAAARVTAIL

Gene : HepCla Segment# : 130 Offset : 1936 1st Codon : 1

Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TAGETCCCCGAAGGGATGCCGCTGACGGAGGCGATCAGTGG

Gene : HepCla Segment# : 131 Offset : 1951 1st Codon : 1

Gene : HepCla Segment# : 132 Offset : 1966 1st Codon : 1

I S S E C T T P C S G S W L R D I W D W I C B V L S D F K T ATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGTATGGAGTCTGTAGGGTCCTGTCCGACTTTAAGACA

Gene : HepCla Segment# : 133 Offset : 1981 1st Codon : 1

D I W D W I C B V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGGGATTGCGAGTGCTCAGCGGATTCCCTTT

Gene : HepCla Segment# : 134 Offset : 1996 1st Codon : 1

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G TGGCTCAAGGCTAAGGCTCAGGCTCCCGGAATCCCTTTCGTCAGGAGAGGCGTATAAGGGAGTGTGGAGGGGAGAGGA

Gene : HepCla Segment# : 135 Offset : 2011 1st Codon : 1

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTGCCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCAT

Gene : HepCla Segment# : 136 Offset : 2026 1st Codon : 1

IMHTRCHCGA BITGHVKNGTMRIVGPRTCR ATCATGCACAAGGTGTCACTGTGGGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

Gene : HepCla Segment# : 137 Offset : 2041 1st Codon : 1

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```
V K N G T M R I V G P R T C R N M W S G T P P I N A Y T T G
 : HepCla
 Segment# : 138
 Offset
       : 2056
1st Codon : 1
 N M W S G T P P I N A Y T T G P C T P L P A P N Y T P A L W
AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCCTCCCCGCTCCCCAATTACACATTCGCTCTGTGG
Gene
       : HepCla
Segment# : 139
Offset
       : 2071
1st Codon : 1
 PCTPLPAPNYTFALWRVSAEBYVEIRRVGD
CCCTGTACCCCTCTGCCTGCCCCCTAACTATACCTTTGCCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT
       : HepCla
Gene
Segment# : 140
Offset
       : 2086
1st Codon : 1
 R V S A B B Y V E I R R V G D F H Y V T G M T T D N L K C P
AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT
       : HepCla
Segment# : 141
Offset
       : 2101
1st Codon : 1
 PHYVTGMTTDNLKCPCQVPSPEFFTELDGV
TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCGGAATTCTTTACCGGACTGGATGGCGTC
Gene
       : HepCla
Segment# : 142
       : 2116
1st Codon : 1
 C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E
Gene
       : HepCla
Segment# : 143
Offset
       : 2131
1st Codon : 1
R L H R F A P P C K P L L R E B V S F R V G L H B Y P V G S
AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGAGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCC
Gene
       : HepCla
Segment# : 144
Offset
      : 2146
1st Codon : 1
EVSFRVGLHEYPVGSQLPCBPEPDVAVLTS
GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGATGTGGCTGTGCTCACCTCC
       : HepCla
Segment# : 145
Offset
      : 2161
1st Codon : 1
Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R
CAGCTCCCCTGTGAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA
       : HepCla
Segment# : 146
Offset
      : 2176
1st Codon : 1
M L T D P S H I T A B A A G R R L A R G S P P S M A S S S A
: HepCla
Segment# : 147
Offset
      : 2191
1st Codon : 1
RLARGSPPSMASSSASQLSAPSLKATCTAN
AGGCTCGCCAGAGGCTCCCCCCTAGCATGGCCTCCAGCTCCCGCCTCCCCGCAGCCCCCCTGAAAGCCACATGCACAGCCAAT
```

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Gene : HepCla Segment# : 148 Offset : 2206 lst Codon : 1

S Q L S A P S L K A T C T A N H D S P D A B L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCGGAACTGATTGAGGCTAACCTCCTGTGG

Gene : HepCla
Segment# : 149
Offset : 2221
lst Codon : 1

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGAGCTCCTCGAGCCCAATCTGCTCTGGGGGCGAGAATGGGGGGGCCAATATCACAAGGGTCGAGTCCGAGAAT

Gene : HepCla Segment# : 150 Offset : 2236 lst Codon : 1

R Q B M G G N I T R V E S E N K V V I L D S F D P L V A B B AGGCAAGAGATCGGCGGAAACATTACCAGAGTGGAAAGCGAAAACTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

Gene : HepCla Segment# : 151 Offset : 2251 lst Codon : 1

Gene : HepCla Segment# : 152 Offset : 2266 1st Codon : 1

DEREISVPAEILRKSRRFAQALPVWARPDY GACGAAAGGGAAATCTCCGTGCCTGCCGAAATCCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

Gene : HepCla Segment# : 153 Offset : 2281 1st Codon : 1

R R F A Q A L P V W A R P D Y N P P L V B T W K K P D Y E P AGGAGATTCGCTCAGCCTCTGTCTGTCGAGACAAAAGCCTGACCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

Gene : HepCla Segment# : 154 Offset : 2296 1st Codon : 1

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCCTGGGAAACCTGGAAACCCGATTACGAACCCCCTTTGGTCCACGGATGCCCTCTGCTCCCCCCTAGGTCCCCCCCT

Gene : HepCla Segment# : 155 Offset : 2311 1st Codon : 1

PVVHGCPLPPPRSPPVPPPKKRTVVLTES
CCCGTCGTCGAGAGGCCTCCCGAGAAGCACAGAGGAGAGAAAGGACAGTGGTCCTGACAGAGCC

Gene : HepCla Segment# : 156 Offset : 2326 1st Codon : 1

V P P P R K K R T V V L T E S T L S T A L A E L A T K S F G GTGCCTCCCCCTAGGAAAAAGGGAACCGTCGTCCACCGAAAGCCACCTCTCCGCACCTCTCGCGAAGCCTCTCGCAAAGTCCTTCGGA

Gene : HepCla Segment# : 157 Offset : 2341 1st Codon : 1

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCAACACCTCCCAACCTCCCCACCTCCGGCATACCGGAGACAATACCACAACCTCC

Gene : HepCla Segment# : 158 Offset : 2356

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1st Codon : 1 S S S T S G I T G D N T T T S S E P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA : HepCla Segment# : 159 Offset : 2371 1st Codon : 1 SEPAPSGC'PPDSDAESYSSMPPLEGEPGDP AGCGAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCT : HepCla Segment# : 160 Offset : 2386 1st Codon : 1 S Y S S M P P L B G B P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCCTCGAGGGGGGGGGCCTGGCGATCCCGATCTGTCCGACGGAGCTGGAGCACAGTGTCCAGCGAAGCCGGA Gene : HepCla Segment# : 161 Offset : 2401 1st Codon : 1 D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA Gene : HepCla Segment# : 162 Offset : 2416 1st Codon: 1
T B D V V C C S M S Y S W T G A L V T P C A A E B Q K L P I ACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATT : HepCla Segment# : 163 Offset : 2431 1st Codon : 1 A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT Gene : HepCla Segment# : 164 Offset : 2446 1st Codon : 1 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T ANGECTETECANCTECTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGGGCTTGCCAAAGGCAAAGGAAAGTGACA Gene : HepCla Segment# : 165 Offset : 2461 1st Codon : 1 S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y O D V L AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC Gene : HepCla Segment# : 166 Offset : 2476 1st Codon : 1 FDRLQVLDSHYQDVLKBVKAAASKVKANLL TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC Gene : HepCla Segment# : 167 Offset : 2491 1st Codon : 1 K B V K A A A S K V K A N L L S V B E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA Gene : HepCla Segment# : 168 : 2506 Offset S V B B A C S L T P P H S A K S K F G Y G A K D V R C H A R AGCSTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGAAGGATGTGAGATGCCATGCCAGA

## 127/216

Gene : HepCla Segment# : 169 : 2521 Offset 1st Codon : 1 SKFGYGAKD V R CHARKAVAHINSV W KD L LE AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA Gene : HepCla Segment# : 170 Offset : 2536 1st Codon : 1 K A V A H I N S V W K D L L E D S V T P I D T T I M A K N E AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATCGCCAAAAACGAA Gene : HepCla Segment# : 171 : 2551 Offset D S V T P I D T T I M A K N B V F C V Q P B K G G R K P A GACTCCGTGACACCCATTGACACCATTATGGCTAAGAATGAGGTCTTCTGTGCAACCCGAAAAGGGGAGGCAGAAAGCCTGCCAGA Gene : HepCla Segment# : 172 Offset : 2566 1st Codon : 1 V F C V Q P B K G G R K P A R L I V F P D L G V R V C B K M GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG : HepCla Gene Segment# : 173 Offset : 2581 1st Codon : 1 LIVPPDLGVRVCBKMALYDVVSKLPLAVMG CTGATTGTGTTTCCCGATCTGGGAGTGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGA : HepCla Segment# : 174 Offset 1st Codon : 1 A L Y D V V S K L P L A V M G S S Y G P Q Y S P G Q R V E P GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAACGGTCGAGTTT Gene : HepCla Segment# : 175 : 2611 Offset 1st Codon : 1 SSYGFQYSPGQRVEFLVQAWKSKKTPMGFS AGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATTCCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC : HepCla Gene Segment# : 176 Offset : 2626 1st Codon : 1 CTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT Gene : HepCla Segment# : 177 Offset : 2641 1st Codon : 1 Y D T R C F D S T V T E S D I R T E E A I Y Q C C D L D P Q Gene : HepCla

Segment# : 178 Offset : 2656 1st Codon : 1

Gene : HepCla Segment# : 179

128/216 Offset : 2671 1st Codon : 1 ARVAIKS LTBRLYVGG PLT NS RGBNCG Y RR GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA Gene : HepCla Segment# : 180 Offset : 2686 1st Codon : 1 G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATACAGAAGGTGTAGGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC Gene : HepCla Segment# : 181 Offset : 2701 1st Codon : 1 C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTTGCCTT Gene : HepCla Segment# : 182 Offset : 2716 1st Codon : 1 T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGATT : HepCla Segment# : 183 Offset : 2731 1st Codon : 1 Q D C T M L V C G D D L V V I C B S A G V Q B D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT Gene : HepCla Segment# : 184 : 2746 1st Codon : 1 C E S A G V Q B D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT Gene : HepCla Segment# : 185 Offset : 2761 F T B A M T R Y S A P P G D P P Q P R Y D L E L I T S C S S TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCTTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCC Gene : HepCla Segment# : 186 Offset : 2776 1st Codon : 1 P Q P E Y D L E L I T S C S S N V S V A H D G A G K R V Y Y CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT Gene : HepCla Segment# : 187 Offset : 2791 1st Codon : 1 N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A N B AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAA : HepCla Gene Segment# : 188 Offset : 2806 1st Codon : 1 LTRDPTTPLARAWETARHTPVNSWLGNII CTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACAGCCAGACACCCCGTCAACTCCTGGCTCGGCAATATCATT Gene : HepCla Segment# : 189 Offset : 2821

Figure 26 (Cont)

TARHTP V N S W L G N I I M F A P T L W A R M I L M T H

1st Codon : 1

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# ${\tt ACCGCTAGGCATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT}$

Gene : HepCla Segment# : 190 Offset : 2836 1st Codon : 1

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC

Gene : HepCla Segment# : 191 Offset : 2851 1st Codon : 1

Gene : HepCla Segment# : 192 Offset : 2866 1st Codon : 1

Gene : HepCla Segment# : 193 Offset : 2881 1st Codon : 1

L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGGAGAGTTAACAGAGTGGCTGCCTGT

Gene : HepCla Segment# : 194 Offset : 2896 1st Codon : 1

L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R CTGCATAGCTTAGGCCTGGCGAAATCAGTAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA

Gene : HepCla Segment# : 195 Offset : 2911 1st Codon : 1

LRKLGVPPLRAWRHRARSVRARLLARGGRAAGCTGGAGAGCTGGTCGCCAGAGGCGGAAGGGCTAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCT

Gene : HepCla Segment# : 196 Offset : 2926 1st Codon : 1

ARSVRARLLARGGRAAICGKYLFNWAVRTKGCCAGAAGCGTCAGGGCTCAGGGCTGTGAGAGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

Gene : HepCla Segment# : 197 Offset : 2941 1st Codon : 1

A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S GCCATTTGCGGAAAGTTATCTGTTTAACTGGGCCGTCAGGACAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

Gene : HepCla Segment# : 198 Offset : 2956 1st Codon : 1

Gene : HepCla Segment# : 199 Offset : 2971 1st Codon : 1

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

Gene : HepCla

#### 130/216

Segment# : 200 Offset : 2986 1st Codon : 1

Gene : HepCla Segment# : 201 Offset : 3001 1st Codon : 1

L A A G V G I Y L L P N R A A CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

Segments in scrambled order:

------

HepCla #77

V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P GTGATTCCCGTCAGGGGAGGCCCCTCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGGGGAGGCCCT

HepCla #68

ARRGREILLGPADGMVSKGWRLLAPITAYA

HepCla #143

R L H R F A P P C K P L L R B B V S F R V G L H B Y P V G S AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGGGAAGTGTCCTTCAGAGTGGACTGCATGAGTATCCCGTCGGCTCC

HepCla #66

V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGCCGATATCATTAACGGACTGCCTGTGCC

HepCla #79

L L C P A G H A V G I F R A A V C T R G V A K A V D F I P V CTGCTCTGCCCTGCCCGACAGGGGACTGCTGTGGATTTCATTCCCGTC

HepCla #113

C V V I V G R I V L S G K P A I I P D R E V L Y R B F D B M
TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGGTCCTGTATAGGGAATTCGATGAGATG

HepCla #139

PCTPLPAPNYTFALWRVSAEEYVBIRRVGDCCCTGTACCCCTGCCCCTAACTATACCTTTGCCCTCTGGGGGGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGTCGGCGAT

HepCla #174

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V B F GCCTCTACGATGTGGCTCAGCAAACGGTCGAGGTTT

HepCla #57

ISWCLWWLQYFLTRVBAQLHVWVPPLNVRG ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA

HepCla #51

ENLVILNAASLAGTHGLVSFLVFFCFAWYL

HepCla #193

LPPIIQRLHGLSAFSLHSYSPGBINRVAACCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCCCCCTTATCCCACGGACGAGATTAACAGAGTGGCTGCCTGT

HepCla #154

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCCTGGGAAACCTGGAAGAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCT

HepCla #48

G V G S S I A S W A I K W E Y V V L L F L L L A D A R V C S GGGGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC

HepC1a #37

L N N T R P P L G N W F G C T W M N S T G F T K V C G A P P CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT

HepCla #185

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S

## 131/216

TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGCTGAGCTCATCACAAGCTGTAGCTCC

HepCla #54

HepCla #70

QQTRGLLGCIITSLTGRDKNQVEGEVQIVS CAGCAAACCAGAGGCCTCCTGGGAGGCTCCAGATTGTGTCC

HepCla #82

HepCla #104

N T P G L P V C Q D H L B F W B G V P T G L T H I D A H F L AACACACCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTCGCGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

HepCla #26

V L L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTCGCTGACGCCTGAGACACCTCCGGAGGCCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC

HepCla #110

HepCla #56

HepCla #197

A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

HepCla #25

I À Y F S M V G N W A K V L V V L L L F A G V D A E T H V T ATCECTTACTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA

HepCla #147

HepCla #52

G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCCGGAGCCGTCTACGCTCTGTATGCCATG

HepCla #145

Q L P C B P E P D V A V L T S M L T D P S H I T A B A A G R CAGCTCCCCTGTGAGCCTGACGCCGTCCTGCCAGACCCTGCCAGACCCCTAGCCATATCACGCCGAAGCCGCTGGCAGA

HepCla #171

D S V T P I D T T I M A K N E V F C V Q P E K G G R K P A R GACTCCGTGACACCCATTGACACCAACCATTATGGCTAAGAATGAGGTCTTCTGTGCAACCCGAAAAGGGAGGCAGGAAAGCCTGCCAGA

HepCla #84

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGGATCCCTCGTGCTGCCCCACACTGGGATCGGAGCCTATATGTCCAAGGCTCACGGA

HepCla #14

HepCla #175

S S Y G F Q Y S P G Q R V B F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATTCCTCCTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC

HepCla #67

HepCla #148

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

## 132/216

HepCla #120

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G. AACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCACACGCCAAACCCTCCTGTTTAACATTCTGGGA

HepCla #176

L V Q A W K S K K T P M G F S Y D T R C F D S T V T B S D I CTGGTCCAGGCTTGGAAAAGACACACCCATGGCTTTAGCTATGACACAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

HepCla #152

D B R B I S V P A B I L R K S R R F A Q A L P V W A R P D Y GACGAAAGGGAAATCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

HepCla #190

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGITTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAGCCCTC

HepCla #96

S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D
AGCGTCATCCCTACCTCCGCGATGTGGTCGTCGTCGCCACAGACGCTCTTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT

HepCla #94

CHSKKKCDBLAAKLVALGINAVAYYRGLDV TGCCATAGCAAAAAGAAATGCGATGAGCTCGCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC

HepCla #46

HepCla #53

K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y AAGGGAAGGTGGGTGCTGGCTCTGTGTTGTGCCTCTGGCTCTGGGAGAGCCTAT

HepCla #87

S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D B C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT

HepCla #196

HepCla #170

KAVAHINSVWKDLLEDSVTPIDTTIMAKNB AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCGCTCGAGGATAGCGCCCTATCGATACCACAATCATGGCCAAAAACGAA

HeoCla #35

F T P S P V V V G T T D R S G A P T Y S W G A N D T D V F V TTCACACCCTCCCCGTGGTGGTCGGCACACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC

HepCla #16

PGCVPCVREGNASRCWVANTPTVATRDGKLCCCGGATGCCTCCCCTGTGTGAGAGGGGAAACGCTAGCAGATGCTGGTGACACCCACAGTGGCTACCAGAGACGGAAAGCTC

HenCla #183

Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

HepCla #125

VAGALVAPKIMSGEVPSTEDLVNLLPAILS GTGGCTGGCGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCCTGCCATTCTGTCC

HepCla #177

HepCla #103

BLTPABTTVRLRAYMNTPGLPVCQDHLBFWGAGCTCACCCTGCCAAACCCATGAGACCATCTGGAATCTGG

HepCla #186

PQPBYDLBLITSCSSNVSVAHDGAGKRVYYCCCCAACCCGAATACGATCTGCAACACGATTACCTCCTCCTCCAGCAATGTCTCCTGCCCAACACGCCCTGCCAAAAGGGTCTACTAT

#### 133/216

HepCla #9

L G K V I D T L T C G F A D L M G Y I P L V G A P L G G A A CTGGGAAAGGTCATCGATCCCTCACCTGTGGCTTTGCCGATCTGATGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT

HepCla #93

A I P L E V I K G G R H L I F C H S K K K C D E L A A K L V GCCATTCCCTCGAGGTCATCAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAGTGTGACGAACTGGCCGAACTGGTC

HepC1a #112

G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGATGCTCGCCGCTCTGGCTCCTCCTCCGCCAACCCGCT

HepCla #184

C B S A G V Q B D A A S L R A F T B A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

HepC1a #199

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

HepCla #158

S S S T S G I T G D N T T T S S B P A P S G C P P D S D A B AGCTCCAGCACAAGCGGATCCCCAGAAGCGGATCCCCCATAGCGGATCCCGAGCGCTCCCCCTAGCGGATCCCCCCATAGCGATCCCGAA

HepCla #100

RTQRRGRTGRGKPGIYRFVAPGBRPSGMPD

HepC1a #43

V R M Y V G G V B H R L B A A C N W T R G B R C D L B D R D
GTGAGAATGTATGTGGGAGGGTGCATAGGCTGAGGTTGACCTGAGGATAGGGAT

HepCla #58

BAQLHVWVPPLNVRGGRDAVILLMCVVHPT GAGGCTCAGCTCCGCTCTGGATGTGAATGTGAATGTGAAGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTCCATCCCACA

HepCla #4

L G V R A T R K T S B R S Q P R G R R Q P I P K A R R P B G CTGGGAGTGAGAGCCACACACAGAGAGACCCTCGAGAGAGCCAACCCAGAGGCAACCCATTCCCAAAGCCAGAAGGCATTCAGGGA

HepCla #187

N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W E AACGTCAGCGCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTTCCACACCCCTCGCCAGAGCCGCTTGGGAA

HepCla #159

SEPAPSGCPPDSDAESYSSMPPLEGGEPGDP AGCGAACCCGCTCCCCCCTCGACTCCCACCCTAGTCCTACTCCAGCATGCCCCCTCTGGAAGCCGAACCCGGAGACCCT

HepCla #63

I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT

HepCla #126

PSTBDLVNLLPAILSPGALVVGVVCAAILR CCCTCCACCGAAGACCTCGTGATCTCCCCCGCTATCCTCAGCCCTGGCGCTCTGGTGGGAGTGGTCTGCGCTGCCATTCTGAGA

HepCla #24

HepCla #7

HepCla #21

WTTQGCNCSIYPGHITGHRMAWDMMMNWSPTGGACAAGCCCAAGGCTGTAACTGAGCATTACCTGGCCATATCACAGGCCATAGGATGGCCTTGGGACATGATGATGAACTGGAGCCCT

HepCla #17

HepCla #42

#### 134/216

HepCla #172

HepCla #10

M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGGCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT

HepCla #27

HepCla #13

L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P CTGGCTCTGCTCAGCAGTGCCTGCCTCCGCCTATCAGGTTAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT

HepCla #71

G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGTGCAAATCGTCAGACACACGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT

HepCla #18

HepCla #83

H A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V CACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATGCGTCCAGGGATACAAAGTGCTCGTGACCCTAACCCTAGCGTC

HepCla #6

HepCla #162

T B D V V C C S M S Y S W T G A L V T P C A A E B Q K L P I ACCGAAGACGTCGTGTCGTCGTCGTCGTCGTCGTCGCTGCCGAAGAGCTCCCCATT

HepCla #55

A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y GCCCTCGACACAGAGGTCGCCGCTAGCTCGCCGAGTGGTCCTCGTCGGCCTCATGGCTCTGACACACTGTCCCCCTATTACAAAAGGTAT

HepCla #38

HepCla #168

S V E B A C S L T P P H S A K S K F G Y G A K D V R C H A R AGCGTCGAGGAAGCCTGTAGCCTCACCCCCCCCCATAGCGCTAAGGTTCGCGTTTTGGCTATGGCGTAAGGATGTGAGATGCCATGCCAGA

HepCla #119

I S G I Q Y L A G L S T L P G N P A I A S L M A P T A A V T ATCTCCGGCATTCAGTATCTGGCTGGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATGGCTTTCACAGCCGCTGTGACA

HepCla #3

Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P CAGATTGTGGGAGGGGTTACCTCCTGCCTAGGAGAGGCCCTAGGCTCAGGGTTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

HepCla #194

L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R CTGCATAGCCTATAGCCCTGGGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA

HepCla #189

T A R H T P V N S W L G N I I M F A P T L W A R M I L M T H ACCGCTAGGCATACCCCTGTGAATAGCTGGCTGGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT

нерCla #81

ENLETTMRSPVFTDNSSPPAVPQSPQVAHL GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

HepCla #91

ATPPGSVTVPHPNIEEVALSTTGEIPFYGK

#### 135/216

GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA

HepCla #60

L V F D I T K L L L A V F G P L W I L Q A S L L K V P Y F V CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGCTCTTCGGACCCCCTCTGGATCTCCGAAGCCTCCTGCTCAAGGTCCCCTATTTCGTC

HepCla #23

T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G ACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCCATTGGGGAGTGCTCGCCGGA

HepCla #98

C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S
TGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACAATCGAAACCACACCCTCCCCCAAGACGCTGTGTCC

HepCla #109

H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACACCCTGTGACAAAGTATATCATGACCTGT

HepCla #179

A R V A I K S L T B R L Y V G G P L T N S R G B N C G Y R R GCCAGAGTGGCTATCACAAAAGCCTCACCGAAAAGCCTCACCGAAAAGCCTCACCGAAAAGCCTCACCGAAAACTGTGGCTATAGGAGA

HenCla #39

C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G
TGCGTCATCGGAGGCGCTGGCAATAACACCTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA

HenCla #76

T C G S S D L Y L V T R H A D V I P V R R R G D S R G S L L ACCTGTGGCTCCAGGGGTTCTGTACCAGAGAGGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGGAGAGGGGGATAGCAGAGGCTCCCTGCTC

HepCla #138

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCCAATTACACATTCGCTCTGTGG

HepCla #89

H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAACCGGACCGGACCGGAGCCAGACTGGTCCTCGCACA

HepCla #130

HepCla #8

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

HepCla #33

HepCla #115

B B C S Q H L P Y I B Q G M M L A E Q P K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

HepCla #107

Y Q A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L TACCAAGCCACAGTGTGTGCCAGGCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC

HepCla #34

HepCla #131

HepCla #161

D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGCTCCACCGTCAGCTCCGAGCCTGGCACAGAGGATGTGGTCTGTTGCATGAGCTATAGCTGGACCGGA

HepCla #108

W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N
TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT

#### 136/216

HepCla #116

L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V Q T N CTGGCTGAGCAATCAACAGAAGCCCTCGGCCTCCTGCAAACCGATACCGCTGAGACAGCTGAGGCTAGCGTCATCCCGCTGTGCAAACCAAT

HepCla #118

WQKLEVPWAKHMWNFISGIQYLAGLSTLPG TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

HepCla #129

L I A F A S R G N H V S P T H Y V P E S D A A A R V T A I L CTGATTGCCTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTGAGGGTCACCGCTATCCTC

HenCla #19

A T L C S A L Y V G D L C G S V F L V G Q L F T F S P R R H GCCACACTGTGTAGCGCTCTGTGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACACCTCTTCACATTCTCCCCCAGAAGGCAT

HepCla #102

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCTCTCGCGAATGCTATGACGCTGGCTGCTGCTACGACTGACACCCCGCTGAGACAACCGTCAGGCTCAGGCTTACATG

HepCla #122

G W V A A Q L A A P G A A T A F V G A G L A G A A I G S V G GGCTGGGTGGCTGCCCAACTGGCTGCCCCTGGCGCTTGTGGAGCCGGACTGGCTGCCGCTGCCCATTGGCTCCCTGGGA

HepCla #29

S W H I N S T A L N C N B S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAAT

HepCla #164

N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T AACGCTCTGTCCAACTCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCACTGCCAAAGGCAAAGGAAAGGAAAGTGACA

HepCla #1

A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G GCCCCTATGTCCCCCAACCCCAAACCCCAAAACCAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACCTCAAGTTTCCCGGAGGCGGA

HepCla #106

HepCla #36

A PTYSWGANDTDVFVLNNTRPPLGNWFGCTGCCCCTATGGGAAACTGGTTCGGATGCACAA

HepCla #156

V P P P R K K R T V V L T E S T L S T A L A E L A T K S F G GTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTCCTCCCCCAAAGCACACTGTCCACCGCTCTGCCTCGAGACCCCACAAAGTCCTTCGGA

HepCla #165

S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y Q D V L AGCACAACCTCCAGGTCCGCCTCTAGAGACAGAGAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCACTATCAGGATGTGCTC

HepCla #90

D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E GACCAAGCCGAAACCGCTGGCGCTGGCTCCCGGCTACCGCTACCGCTACCCCTCCCGGAAGCGTCACCGCTCCCCATCCCAATATCGAA

HepCla #141

FHYVTGMTTDNLKCPCQVPSPEFFTBLDGV

HepCla #198

LKLTPIAAAGRLDLSGWFTAGYSGGDIYHS

HepCla #117

A S R Q A E V I A P A V Q T N W Q K L E V P W A K H N W N F GCCTCCAGGCAAGCGAAGTGATTGCCCCTCCCGCCCTCCAGACAAACTGGCAGAGTGTTTTTGGGCTAAGCATATGTGGAACTTT

HepCla #181

#### 137/216

HepCla #166

PDRLQVLDSHYQDVLKEVKAAASKVKANLL TTCGATAGGCTCCAGGTCCTGGATAGCCATACCAAGACGTCCTGAAAGAGGTCAAGGTCAAGGTCAAAGTGAAAGCCAATCTGCTC

HepCla #180

G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCACAAGCTGTGGCAATACCCTC

HepCla #136

I M H T R C H C G A E I T G H V K N G T M R I V G P R T C R ATCATGCACACAGGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

HepCla #144

EVSFRVGLHEYPVGSQLPCEPEPDVAVLTS
GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCC

HepCla #167

K B V K A A A S K V K A N L L S V B B A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCCTCACTCCGCCAAA

HepCla #59

G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGGAGACGCTGTGTTGTGTCTCTGGTCCTCCTGGTGTTTTGACCATACCTAAACTGCTCCTGGCTGTTTTGGCCCT

HepCla #146

HepCla #78

S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A AGCCCTAGGCCTATCTCCTAAGGGAAGCTCCGGGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

HepCla #32

D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTITGACCAAGGCTGGGGCCCTATCTCCTAGGCATAGCGTAGCGTATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT

HepCla #128

HepCla #50

CLWMMLLISQABAALBNLVILNAASLAGTH TGCCTCTGGATGATGCTCTGATTAGCCAAGCCGCAGCCCTCGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCAGACCCAT

HepCla #114

I I P D R E V L Y R E P D E M E E C S Q H L P Y I E Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG

HepCla #47

L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y
CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT

HepCla #200

HepCla #85

A A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA

HenCla #6

R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCCGCGCCT

HepCla #153

R P A Q A L P V W A R P D Y N P P L V B T W K K P D Y B P AGGAGATTCGCTCAGGCTCTGGCCTGTGGGCCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

HepCla #72

TAAQTPLATCINGVCWTVYHGAGTRTIASPACCGCTGCCCAAACCTTCTGGCTACCATGGCCCTACCATGGCGCTCGCACAAGGACAATCGCTAGCCCT

HepCla #65

#### 138/216

W A H N G L R D L A V A V E P V V F S Q M E T K L I T W G A TGGGCTCACAATGGCCTCAGGGACCTGTGGCTGTGGCACCCGTCGTGTTTAGCCAAATGGAACCAAACTGATTACCTGGGGCGCT

HepCla #74

HepCla #151

HepCla #64

LTGTYVYNHLTPLRDWAHNGLRDLAVAVEP CTGACAGGCACATACGTCTACATCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGAGCCT

HepCla #80

V C T R G V A K A V D F I P V B N L B T T M R S P V F T D N GTGTGTACCAGAGGGGTCGCCAAAGCCGTCGACATTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

HepCla #95

ALGINAVAYYRGLDVSVIPTSGDVVVVATDGCCCTCGGCATTAACGCTGTGGCTACTAATAGGGGACTGGATGTCTCCGTGATTCCCACAAGCGGAGACGTCGTGGCTACCGAT

HepCla #111

HepCla #97

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACGGCTATACCGGGGGACTTTGACTCCGTGATTGACTACACGTCGTCACCCCAAACCGTCGACTTTAGCCTCGACCCT

HepCla #2

N T N R R P Q D V K F P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

HepCla #11

R A L A H G V R V L B D G V N Y A T G N L P G C S F S I F L AGGGCTCTGGCTCACGGAGTGAGGATGCTCGAGGATGTGCCTCACCTAGCATTTTCCTC

HepCla #169

S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L R AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTCACGCTAGGAAAGCCGTCGCCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA

HepCla #28

T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC

HepCla #30

N T G W L A G L F Y Q H K F N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCTGGCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGATGAGAACTGACA

HepCla #49

HepCla #192

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC

HepCla #73

W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTTGGATTCAGATGTACACAAACGTCGACCAAGACCTC

HepCla #101

Y R F V A P G B R P S G M F D S S V L C B C Y D A G C A W Y TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTTACGATGCCGGATGCGCTTGGTAT

HepCla #45

R S B L S P L L L S T T Q W Q V L P C S F T T L P A L S T G
AGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCTCTTCACAACCCTCCCGGTCTGTCCACCGGA

HepCla #195

LRKLGVPPLRAWRHRARSVRARLLARGGRA

#### 139/216

CTGAGAAAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGGCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCT

HepCla #121

S P L T T S Q T L L P N I L G G W V A A Q L A A P G A A T A AGCCCTCTGACAACCTCCCAGACACTGCTCTCAATATCCTCGGGGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

HepCla #61

LWILQAS LLKVPYFVRVQGLLRICALARKM CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTTGTGAGAGTGCAAGAGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG

HepCla #137

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAACGGAACCTTGGGGATCCTGGGACCCTGGGACCTTGCGGACCTGCGGACCTTTCCCATTAACGCTTACACAACCGGA

HepCla #92

EVALSTTGBIPFYGKAIPLBVIKGGRHLIPGAGGTCGCCCTCAGCACACCAGAGAGAGACTCCTCTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT

HepCla #188

HepCla #140

R V S A B B Y V B I R R V G D F H Y V T G M T T D W L K C P AGGGTCAGCGCTGAGAGAATACGTCGAGATTAGGAGAGTGGGAGAGTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

HepCla #155

PVVHGCPLPPPRSPPVPPPRKKRTVVLTES

HepCla #157

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCGAACTGCCTACCAAAAGCTTTGGCTCCAGCTCCAGCATTACCGGAGACAATACCACAACCTCC

HepCla #135

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H
GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGCCATTATGCATACCAGATGCCATTGCGAAGCCGAAATCACAGGCCAT

HepCla #20

V P L V G Q L P T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATT

HepCla #123

FVGAGLAGAAIGSVGLGKVLVDILAGYGAG TTCGTCGGCGCTCGCCGGAGCCCCTATCGGAAGCGTCGGCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCCGGA

HepCla #133

D I W D W I C B V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGCAGAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCTGGCATTCCCTTT

HepCla #15

N S S I V Y B A A D A I L H T P G C V P C V R B G N A S R C AACTCCAGCATTGTGTGTGTGTGTGTGTGTGTGTGGGTAGGGAAGGCAATGCCTCCAGGTGT

HepCla #31

SSGCPBRLASCRRLTDFDQGWGPISYANGS AGCTCCGGCTGTCCCGAAAGGCTCCTGCAGAAGGCTCACCGATTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC

HepCla #178

HenCla #69

V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGGACTGCTCGCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA

HepCla #191

FFSVLIARDQLEQALDCEIYGACYSIEPLD

HepCla #142

C Q V P S P B P F T B L D G V R L H R P A P P C K P L L R B TGCCAAGTGCCTAGCCCTGAGTTTTCCCAGGAGCTCGACGGAGAGCTGCATAGGTTTGCCCCTCCTGTAAGCCCTCTGCTCAGGGAA

## 140/216

HepCla #182

T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAGGCTAGGGCTGCCTGTAGGCCTGCCAGACTGTACCATGCTGGTCTGGGAGACGATCTGGTCGTGATT

HepCla #86

IDPNIRTGVRTITTGSPITYSTYGKPLADG ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCATACCGCAATACCGAAAGTTTCTGGCTGACGGA

HepCla #44

C N W T R G B R C D L B D R D R S E L S P L L L S T T Q W Q TGCAATTGGCAAGGGGAGGGGAGACGGAGACGGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA

HepCla #22

T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCEGACACAGAATEGCTTGGGATATGATGATTGATTGATTCCTCAGGCTCTTGGTCATTGCTCAGGCTCTTGAGAATCCCTCAGGCT

HepCla #127

PGALVVGVCAAILRRHVGPGEGAVQWMNRCCCCGGAGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCGAAGGCCCTCGCAATGGATGAACAGA

HepCla #149

H D S P D A B L I E A N L L W R Q E M G G N I T R V E S B N CACGATAGCCCTGACGCTGAGCCCATCTGAGCCCATCTGCTCTGAGACAGGAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAAT

HepCla #105

B G V F T G L T H I D A H F L S Q T K Q S G B N F P Y L V A GAGGGAGTGTTTACCGGACTGACACACACTTGACGCTCACTTCTCTCCCAGACAAAGCAAAGCGAGAATTTCCCTTACCTCGTGGCT

ReoCla #5

RGRRQPIPKARRPEGRTWAQPGYPWPLYGN AGGGGAAGGACAGCCTAACCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT

HepCla #173

LIVFPDLGVRVCEKMALYDVVSKLPLAVMG

HeoCla #12

HepCla #124

L G K V L V D I L A G Y G A G V A G A L V A F K I M S G E V CTGGGAAAGGTCCTGGCGTCGACATTCTGGCTGGCTATGGCGGAGGCCCTCGTGGCTTTCAAAATCATGAGGGGAGAGGTC

HepCla #160

S Y S S M P P L E G B P G D P D L S D G S W S T V S S E A G
AGCTATAGCTCCATGCCTCCCTCGAGGGAGGCCTGGCGATCCCGATCTGTCCGACGGAGCTGGGGAGCACAGTGTCCAGCGAAGCCCGA

HepCla #150

RQEMGGNITRVESENKVVILDSFDPLVAEE
AGGCAAGAGATGGCGAAAACAAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

HepCla #75

V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D GTGGGATGGCTTCCCCTTCAGGGAAGCCTCACCCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGCCATGCCGATGCCTAT

HeoCla #88

G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC

HepCla #99

T F T I E T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTTTACCATTGAGACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGAGAGCCGGAAGGGGAAAGCCTGGCATT

HepCla #40

D C F R K H P B A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAACCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTCGACTATCCCTAT

HepCla #201

LAAGVGIYLLPNRAA

## 141/216

HepCla #163

A L V T P C A A B E Q K L P I N A L S N S L L R H H N L V Y
GCCCTCGTGACACCCTGTGCCGCTGACGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT

HepCla #132

ISSECTTPCSGSWLRDIWDWICEVLSDFKT

HepCla #134

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G
TGGCTCAAGGCTAAGGCTCATGCCTCAGGTCCCCGGAATCCCTTTCGTCAGGAGAGGCGTATAAGGGAGTGTGGAGGGGAACGGA

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S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K
AGCEGACCCTEGATCACCACGATGCCTCGTGGATTACCCTTACCACTATCCCTTACCATTACCATTTTCAAA

#### Artificial Protein:

Artificial Protein:

VIPVRRRGDSRGSLLSPRPISYLKGSSGGPARRGREILLGPADGMVSKGWRLLAPITAYARLHRFAPPCKPLLREEVSPRVGLHEYPVGSVVPSQMET KLITWGADTAACGDIINGLPVSLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVCVVIVGRIVLSGKPAIIPDREVLYREFDEMPCTPLPAPNYTFALWR vsaeeyveirrvgdalydvvsklplavmgssygfqyspgqrvefiswclwwlqyfltrveaqlhvwvpplmvrgenlvilmaaslagthglvsflvff CFAWYLLPPI I QRLHGLSAFSLHSYSPGEINRVAACNPPLVETWKKPDYEPPVVHGCPLPPPRSPPGVGSSIASWAIKWEYVVLLPLLLADARVCSLN ntrpplgnnfgctwmnstgftkvcgappftbamtrysappgdppqpbydlblitscsswpllllllalpqrayaldtbvaascggvvlqqtrgligci ITSLTGRDKNQVEGEVQIVSSSPPAVPQSPQVAHLHAPTGSGKSTKVPAANTPGLPVCQDHLEFWEGVFTGLTHIDAHFLVLLLPAGVDAETHVTGGN agrttsglvsllevtlthpvtkyimtcmsadlevvtstwvlvvglmaltlspyykryiswclmwlqyfltrvaicgkylfnmavrtklkltpiaaagr ldlsiaypsmvgnwakvlvvlllpagvdaethvtrlargsppsmasssasqlsapslkatctanglvsplvppcpawylkgrwvpgavyalygmqlpc epepdvavltsmltdpshltabaagrdsvtpidttimaknevfcvqpekggrkparyaaqgykvlvlnpsvaatlgfgaymskahgvrnstglyhvtn DCPNSSIVYEAADAILHTSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSDTAACGDIINGLPVSARRGREILLGPADGMSQLSAPSLKATCTANHDSPD ablieanllwnpaiaslmaftaavtsplitsqtllfniiglvqawkskktpmgfsydtrcfdstvtesdiderbisvpabilrksrrfaqalpvwarp DYMPAPTLNARMILMTHFFSVLIARDQLEQALSVIPTSGDVVVVATDALMTGYTGDFDSVIDCHSKKKCDBLAAKLVALGINAVAYYRGLDVVLPCSF ttlpalstglihlhqnivdvqylykgrwvpgavyalygmwpllllllalpqrayspitystygkpladggcsggaydiiicdbcarsvrarllarggr AAICGKYLFNWAVRTKKAVAHINSVWKDILLEDSVTPIDTTIMAKNEFTPSPVVVGTTDRSGAPTYSWGANDTDVFVPGCVPCVREGNASRCWVAMTPT VATROGKLQDCTMLVCGDDLVVICESAGVQEDAASLRAVAGALVAFKIMSGEVPSTEDLVNLLPAILSYDTRCFDSTVTESDIRTBRAIYQCCDLDPQ eltpaettvrlraymntpglpvcqdhlefwpqpeydlelitscssnvsvahdgagkrvyylgkvidtltcgfadlmgyiplvgaplggaaaiplevik GGRHLIFCHSKKKCDBLAAKLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPACESAGVQBDAASLRAFTEAMTRYSAPPGDPGWFTAGYSGGDIYHSV SHARPRWFWFCLLLSSSTSGITGDWTTTSSEPAPSGCPPDSDAERTQRRGRTGRGKPGIYRFVAPGERPSGMFDVRMYVGGVEHRLEAACNWTRGERC DLEDRDEAQLHVWVPPLNVRGGRDAVILLMCVVHPTLGVRATRKTSERSQPRGRRQPIPKARRPEGNVSVAHDGAGKRVYYLTRDPTTPLARAAWESE PAPSGCPPDSDAESYSSMPPLEGEPGDPIGGHYVQMAIIKLGALTGTYVYNHLTPLRDPSTEDLVNLLPAILSPGALVVGVVCAAILRILDMIAGAHW GVLAGIAYFSMVGNNAKVLVEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNWTTQGCNCSIYPGHITGHRMAWDMMNWSPWVAMTPTVATRDGKLPAT QLRRHIDLLVGSRLWHYPCTINYTIFKVRMYVGGVEHRLEAAVFCVQPEKGGRKPARLIVFPDLGVRVCEKMMGYIPLVGAPLGGAARALAHGVRVLE DGVNGGNAGRTTSGLVSLLTPGAKQNIQLINTNGLALLSCLTVPASAYQVRNSTGLYHVTNDCPGRDKNQVEGEVQIVSTAAQTFLATCINGVCPATQ LRRHIDLLVGSATLCSALYVGDLCGSHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVRTWAQPGYPWPLYGNEGCGWAGWLLSPRGSTEDVVCCSMSYS WTGALVTPCAABBQKLPIALDTEVAASCGGVVLVGLMALTLSPYYKRYWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTSVBBACSLTPPHSAKSKFGY gakdvrcharisg-qylaglstlpgnpaiaslmaptaavtqivggvyllprrgprlgvratrktsbrsqplhsyspgbinrvaaclrklgvpplrawr HRTARHTPVNSWLGNI IMPAPTLWARMILMTHENLETTMRSPVFTDNSSPPAVPQSFQVAHLATPPGSVTVPHPNI EEVALSTTGBI PFYGKLVFDIT  $\textbf{KLLLAVFGPLWILQASLLKVPYFVTAALVMAQLLRIPQAILDMIAGAHWGVLAGCNTCVTQTVDFSLDPTFTIETTTLPQDAVSHGPTPLLYRLGAVQ\\$ nbvtlthpvtkyimtcarvaikslterlyvggplinsrgencgyrrcviggagnntlhcptdcfrkhpbatysrcgicgssdlylvtrhadvipvrrr gdsrgsllnnwsgtfpinayttgpctplpapnytfalwhstdatsilgigtvldqaetagarlvvlatyvpesdaaarvtailssltvtqllrrlhqw RPSWGPTDPRRRSRNLGKVIDTLTCGFADLGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCEECSQHLPYIEQGMMLAEQFKQKALGLLQTYQATVCAR aqapppswdqwwkclirlkptlcgivpaksvcgpvycptpspvvvgttdrsgssltvtqllrrlhowissbcttpcsgswlrdlsdgswstvssbagt edvvccsmsyswtgmdqmwkclirlkptlhgptpllyrlgavqnlaeqfkqkalgllqtasrqaeviapavqtnwqklevfwakhmwnfisgiqylag LSTLPGLIAFASRGNHVSPTHYVPBSDAAARVTAILATLCSALYVGDLCGSVPLVGQLFTFSPRRHSSVLCBCYDAGCAWYBLTPAETTVRLRAYMGW VAAQLAAPGAATAPVGAGLAGAAIGSVGSWHINSTALNCNESLNTGWLAGLPYQHKPNNALSNSLLRHHNLVYSTTSRSACQRQKKVTAAMSTNPKPQ rktkritnrrpodvkppgggsqtkqsgenppylvayqatvcaraqapppsaptyswgandtdvfvlnntrpplgnwfgctvppprkkrtvvltestls TALABLATKSPGSTTSRSACQRQKKVTFDRLQVLDSHYQDVLDQAETAGARLVVLATATPPGSVTVPHPNIEFHYVTGMTTDNLKCPCQVPSPEFFTB ldgvlkltpiaaagrldlsgwftagysggdiyhsasrqaeviapavqtnwqklbvfwakhmwnfcrasgvlttscgwtltcyikaraacraaglfdrl QvldshyQdvlkevkaaaskvkanllgpltnsrgencgyrrcrasgvlttscgntlimhtrchcgabitghvkngtmrivgprtcrbvsfrvglheyp vgsqlpcbpbpdvavltskbvkaaaskvkanllsvbbacsltpphsakgrdavillmcvvhptlvfditklllavpgpmltdpshitabaagrrlarg SPPSMASSSASPRPISYLKGSSGGPLLCPAGHAVGIFRAADFDQGWGPISYANGSGPDQRPYCWHYPPKPRHVGPGEGAVQWMNRLIAFASRGNHVSP THCLWMMLLISQABAALENLVILNAASLAGTHIIPDRBVLYRBPDEMBECSQHLPYIBQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARP rwfwfcllllaagvgiyllpnraaaatigfgaymskahgidpnirtgvrtittgrvqgllricalarkmigghyvqmaiiklgarrfaqalpvwarpd YNPPLVETWKKPDYEPTAAQTFLATCINGVCWTVYHGAGTRTIASPWAHNGLRDLAVAVEPVVFSQMBTKLITWGAKGPVIQMYTNVDQDLVGWPAPQ GSRSLTPCKVVILDSFDPLVAEEDERBISVPAE1LRKSLTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVCTRGVAKAVDP1PVENLETTMRSPVFTDN alginavayyrgldvsviptsgdvvvvatdmsadlbvvtstmvlvggvlaalaayclstgalmtgytgdfdsvidcntcvtqtvdpsldpntnrrpqd vkfpgggqivggvyllprrgprralahgvrvledgvnyatgnlpgcspsiplskfgygakdvrcharkavahinsvmkdlletpgakqniqlintngs WHINSTALNCNESLNTGWLAGLPYQHKFNSSGCPERLASCRRLTVVLLPLLLADARVCSCLWMMLLISQABAALDCEIYGACYSIBPLDLPPIIQRLH GLSAFSWTVYHGAGTRTIASPKGPVIQMYTNVDQDLYRFVAPGERPSGMFDSSVLCECYDAGCAWYRSELSPLLLSTTQWQVLPCSFTTLPALSTGLR klgvpplrawrhrarsvrarllarggrasplttsqtllfnilggwvaaqlaapgaatalwilqasllkvpypvrvqgllricalarkmvkngtmrivg prtcrnmwsgtfpinayttgevalsttgeipfygkaiplevikggrhlipltrdpttplaraambtarhtpvnswlgniirvsabbyvbirrvgdfhy VTG#TTDNLKCPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTLSTALABLATKSFGSSSTSGITGDNTTTSVSCQRGYKGVWRGDGIMHTRCHCGAE itghvflvgqlftfsprrhwttqgcncsiypghifvgaglagaaigsvglgkvlvdilagygagdiwdwicevlsdfktwlkaklmpqlpgipfnssi vyeaadailhtpgcvpcvregnasrcssgcperlascrrltdpdgwgpisyangsrteeaiyoccdldpoarvaikslterlyvgvskgwrllapit AYAQQTRGLLGCI ITSLTPFSVLIARDQLEQALDCEIYGACYS I BPLDCQVPSPEFFTELDGVRLHRFAPPCKPLLRETCYI KARAACRAAGLQDCTM

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LVCGDDLVVIIDPNIRTGVRTITTGSPITYSTYGKFLADGCNWTRGERCDLEDRDRSELSPLLLSTTQWQTGHRMAWDMMNWSPTAALVMAQLLRIP QAPGALVVGVVCAAILRRHVGPGEGAVQMMNRHDSPDABLIEANLLWRQEMGGNITRVESENEGVFTGLTHIDAHFLSQTKQSGENFPYLVARGRRQP IPKARRPEGRTWAQPGYPWPLYGNLIVPPDLGVRVCEKMALYDVVSKLPLAVMGYATGNLPGCSPSIFLLALLSCLTVPASAYQLGKVLVDILAGYGA GVAGALVAFKIMSGEVSYSSMPPLEGEPGDPDLSDGSWSTVSSEAGRQEMGGNITRVESENKVVILDSFDPLVAEEVGWPAPQGSRSLTPCTCGSSDL YLVTRHADGCSGGAYDIIICDECHSTDATSILGIGTVLFFTIETTTLPQDAVSRTQRRGRTGRGKPGIDCFRKHPEATYSRCGSGEWITPRCLVDYPY LAAGYGIYLLPMRAAALVTPCAAEEQKLPINALSNSLLRHNLVYISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYK GVWRGDGSGPWITPRCLVDYPYRLMHYPCTINYTIFK

#### Artificial DNA:

GGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCTACGCTCCACAGATTCG CTCCCCCTTGCAAACCCCTCCTGAGAGAGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCCGTCGTCTTCTCCCAGATGGAGACA CTTTAGGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTCTGGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGC GTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGATGCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGG CTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTTATCTCCTGGTGTCTGTGGTGGTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGT TGCTTTGCCTGGTACCTCCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGT GGCTGCCTGTAACCCTCCCCCCGGAAACCTGGAAGAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCC  $\tt CTGGCGTCGGCTTGCCTGGGGTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAAT$ AACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTCACAGAGGCTAT GACAAGGTATAGCGCTCCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCCTGGCCTCTGCTCCTGCTCCTGC TCGCCCTCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATT GGTCGTGACAAGCACATGGGTCCTGGTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGGCTCTGGTGGCTGC AATACTTTCTGACAAGGGTCGCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCAGA CTGGATCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTTCTGCCGGAGTGGATGCCGAAACCCATGT TOGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGT GAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGA CACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGGATACGCTGCCCAAGGCTATAAGGTCCTGG TCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCACCGGACTGTATCACGTCACCAAT Gactisteccaatagetectatestetaegaageegetigaesetateeteeagaeagaeteetaeggatteeaataeteeeggaeagagagtisgaatt CCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGA GAGGCAGAGAGATTCTGCTCGGCCCTGCCGATGGCCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGAT GCCGAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCTCACCACAAGCCAAAC  ${\tt CCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGA}\\$ GACTATATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCCTCAG CGTCATCCCTACCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGCCATAGCA AAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTCGTGCTCCCCTGTAGCTTT GTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCTCTGCCTCAGAGAGCCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCC TCGCCGATGCCGCATGCTCCGGCGGAGCCTATGACATTATCATTTCCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGA GCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAG CGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAATTCACACCCTCCCCCGTCGTCGTCGCCACAACCGATACGTCCGGCGCTCCCCACATACT GTGGCTACCAGAGACGGAAAGCTCCAGGATTGCACAATGCTCGTGTGTGGGGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGC GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGGCCCCAACC CGANTACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTCTCCGTGGCTCACGATGGCGCAAAAGGGTCTACTATCTGGGAAAGGTCATCG ATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAAA GGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCGCCGCTCTGGCTGCCTATTG CCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGCGAAAGCGCTGCGTTCCAGGAAGACGCTGCCTCCCTGA AGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGGATAACACCACCACAAGCTCCGAGCCTGC GACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCCTCTGAATGTGAGAGGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGT GCATCCCACACTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAAACCCATTCCCAAAGCCAGAAGGCCTGAGG  $\tt CCCGCTCCCTGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCTATCGGAGGCCATTA$ CGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGATCCCTCCACGGAAGACCTCGTGA  $\textbf{ATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGG$ 

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TCAGGGTCTGCGAAAAGATGATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAA GACGGAGTGAATGGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCGGAGCCAAACAGAATATCCAACTGATTAACACAAA CGGACTGGCTCTGACCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCTGGCA GAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACACGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGTCCCGCTACCCAA CTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCTCCCACAGGCTCCGG TGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCGCCGCTAGCTGTGCCGGAGTGGTCCC TTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCACAAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCGCATAGCGCTAAGTCCAAGTTTGGCTAT GGCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGCTACCAGAAAGACAAGCG AAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGA GAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCC CTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTCGATATCACA AAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTCGTGATGGCCCAACT AACGAAGTGACACTGACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACC CCTCACCAATAGCAGAGGCGAAAACTGTGGGTATAGGAGATGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGA CACATTCGCTCTGTGGCACTCCACCGATGCCACAAGCATTCTGGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGC TCGCCACATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG AGGCCTAGCTGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACTGACATGCGGATTCGCTGACCTCGGCCCTGA ATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGA GCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGGAATCGTCCCGCTAAGTCCGTGTGTGG GAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTAC CCCTCTGCTCTACAGACTGGGAGCCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGG TCATCGCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACGTGTGGAATTCATTAGCGGGAATCCAATACCTCGCCGGA CTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGGTCCGACGCTGCCGCTAGGGTCAC GTGGCTGCCCAACTGGCTGCCCCTGGCGCTGCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCGCTTGCCCATTGGCTCCGTGGGAAGCTGGCACATTAA  $\tt CTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACACAAATTCAATAACGCTCTGTCCCAACTCCCTGC$ AGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCT TCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAAACCGTCGTGCTCACCGAAAGCACACTGTCC ACCECTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCTGTCAGAGAAAAAAGGTCACCTTTGACAGACTGCAAGT GCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCG CTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTGGGCTAAGCATATGTGGAACTTTTGCA GAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTCGGCCTCTTCGATAGGCTC CAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAAGGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAG GGGAGAGATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCG CTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGGAGAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCT GTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCT AGCCCTCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGCCCGCTGGCCATGC  $\tt CGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGCCACT$  $\tt ATCCCCCTAAGCCTAGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTCGCTAGCAGAGGCAATCACGTCAGCCCT$ ACCCATTGCCTCTGGATGATGCTCCTGATTAGCCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCCATAT CATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACC TCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCT AGGTGGTTCTGGTTCTGCTCCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCGCTTTGGCGCTTTA CATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGG CTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCTAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCCAGACCCGAT TACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGAC CGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTGTTTTAGCC GATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCG TCGAGCCTGTGTGTACCAGAGGCCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATATGTCCGC

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ATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCCAAACCGTCGACTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGAT GTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGA GGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACG CTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCC TCATCTCCCAGGCTGAGGCTGCCCTCGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCAT GGCCTCAGCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCAAAGGGCCCTGTGATTCAGATGTACACAAACGTCGA ATAGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGGCTCTGTCCACCGGACTGAGA AAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGCCGAAGGGCTAGCCCTCTGACAAC  $\tt CTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCGGGGCCGCTACCGCTCTGTGGATCCTCCAGGCTAGCC$ TCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAACCGAACCATGAGGATTGTGGGA CCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGAGAGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTA CGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTTCTGACAAGGGATCCCACAACCCCTCTGGGTAGGGCTGCCTGGGAGA GTGACAGGCATGACCACAGACAATCTGAAATGCCCTCCCGTCGTGCATGGCTGTCCCCCTCCCCAGAAGCCCCTCCCGTCCCCTCCCAGAAA GAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCG GAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAA ATCACAGGCCATGTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCCTAGGAGACACTGGACCACAGGGGATGCAACTTGCTCCATCTATCCCGGACA CATTTTCGTCGGCGCTGGCCTGGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGGAGACA TTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCATTCCCTTTAACTCCAGCATT GTGTATGAGGCTGCCGATGCCCATTCTGCATACCCCTGGCTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAG GCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCT GTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACA GCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCAACTGGAACAGGCTCT GGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGC ATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAAACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATG CTGGTCTGCGGAGACGATCTGGTCGTGATTATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATA CAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCCACAGCCGCTCTGGTCATGACTAGCTCCTGAGAATCCCT CAGGCTCCCGGAGCCCTCGTGGTGGGGTGTGTGTGCCGCTATCCTCAGGAGACACGTCGGCCGGAGGGCGCTGTGCAATGGATGAACAGACA CGATAGCCCTGACGCTCAGCGCAACCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGT ttaccggactgacacattgacgctcactttctgtcccagacaaagcaaagcgaagaatttcccttacctcgtggctaggggaaggacagcct  $\tt ATCCCTAAGGCTAGGAGACCCGGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTGTTTCCCGATCTGGGAGT$ GAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGATACGCTACCGGAAACCTCCCCGGATGCTCCTTCT GGCGTCGCCCGGAGCCCTCCTGGCTTTCAAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCT GTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCC TACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGG CATTGGCACAGTGCTCACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGCCAGAACCGGAAGGGGAAAGC CTGGCATTGACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCT CAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGA TCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAAGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAG GGAGTGTGGAGGGGAGACGGAAGCCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTA TACCATTTTCAAA

HepC Savine Cassette Sequences (A+B+C) with specific restriction sites removed which can be joined to generate a single expressible open reading frame that encodes the hepc Savine protein above

### Cassette A

## 145/216

CTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAATAACACAA GGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGGGCGCTCCCCCTTTC ACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGAATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTG TAGCTCCTGGCCTCTGCTCCTGCTCCCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTCCCT GCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAG GTCGAGGGAGAGGTCCAGATTGTGTCCAGCTCCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGCCCATCTGCATGCCCC TACCGGAAGCGGAAAGTCCACCAAAGTGCCTGCCGCTAACACACCCGGACTGCCTGTGTGTCAGGATCACCTCGAGTTTT GGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTCGTGCTCCTGCTCTTCGCTGGCGTqGALGCTGAG ACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGAGGTCACCCTCACCCGTCCCGT CACCAAATACATTATGACATGAGCGCTGACCTCGAGGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGG ATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGA TCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCTGTTTGCCGGAGTGGATG COGARACCCATGTGACAAGGCTCGCCAGAGGCTCCCCCCTAGCATGGCCTCCAGCTCCGAGCTCAGCGCTCCC GCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGACACAACCATTATG GCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGT CCTGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCA CCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGC TCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAGTTLCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGG GCCTGCCGATGGCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCGGATGCC GAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCT CACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCCAAAAAGACACCCCATGGGCTTTA CTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCCGTCTGGGCTAGGCCTGACTATATGTTTGCCCCCTACCCTCTGGGC TAGGATGATCCTCATGACACACTTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTCAGCGTCATCCCTA CCTCCGGCGATGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGC CATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCT ALGTCCAGTATCTGTATAAGGGAAGGTGGGTGCCTGGCGCTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTG CTCCTGGCTCTGCGTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTC CGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTACGCTAGGGGAGGCAGAG CCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAG GATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAGTTtACACCCTCCCCGTCGTCGT CGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCC CCTGTGTGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTCCAG GATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCT CAGGGCTGTGGCTGCGCCTTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCC TGCCTGCCATTCTGTCCTACGATACCAGATGCTTTGACTCCACCGTCACCGAAAGCGATATCAGAACCGAAGAGGCTATC TATCAGTGTTGCGATCTcGAcCCCCAAGAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCC TGGCCTCCCGTCTGCCAAGACCATCTGGAqTTLTGGCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTCCTCCCA GCAATGTGTCCGTGGCTCACGATGGCGCTAGCAAAAGGGTCTACTATCTGGGAAAGGTCATCGATACCCTCACCTGTGGC TTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAA AGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCG CCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGC GAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGG AGACCCTGGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTT GGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGC GGATGCCCTCCGGATGCCGAAAGGACACAGAGAAGGGCAAGGCCAGAGGCAAACCCGGAATCTATAGGTT CCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATGAGGTCAGCTCAGGTCTGGGTCCCCCCTCTG AATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACACTGGGAGTGAGAGCCACAAGGAA AACCTCCGAGAGAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGAAACGTCAGCGTCG CCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACCACCACCACCAGAGCCGCTTGGGAAAGC GAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCCTCTGGAAGGCGAACCCGG AGACCCTATGGGGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATC TGACACCCTCAGaGACCCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTG GGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGGGGGGGTCCTGGCTTGCCTA GCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATgtcgactgagaattcgcc

### Cassette B

## 146/216

GCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGG ACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAA ACGATTGCCCTGGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCC ACATGCATTAACGGAGTGTCCCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTC CGCCTCTACGTCGGCGATCTGTGGGCTCCCACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATG GGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTTGCTCCATGTC CTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCG CCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTATTGGATGAAC TCCACCGGATTCACAAAGGTCTGCGGAGCCCCTCCTGTGTGATTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCAC AAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTTCGAGGTTTGGCTATGGCGCTAAGGATGTGAGAT GCCATGCCAGAATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATG GCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCCTAGGCTCGGCGTCAGGGC TACCAGAAAGACAAGCGAAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCA GGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGAACCGCTAGGCATACCCCTGTGAATAGCTGGGTAGACAC ATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCATGAGAATCTGGAAACCACAATGAGAAGCCC TGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCCACACCCCCTGGCTCCG TGACAGTGCCTCACCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGGGAAATCCCTTTCTATGGCAAACTGGTCTTC GATATCACAAAGCTCCTGCTCGCCCTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGT CACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAG TGCTCGCCGGATGCAATACCTGTGTGACACAGACGGGGTTTCTCCCTcGAcCCCACATTCACAATCGAAACCACAACC CTCCCCCAGGACGCTGTGTCCCCACGGACCCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGAC ACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGAC CCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGATGCGTCATCGGAGGGGCGCTGGCAATAACACTGCATTGC CCTACCGATGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGT CACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGGGGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACAT TCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCCAATTACACATTCGCTCTGTGGCACTCCACC GATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGTCGCCAC ATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGAC TGCATCAGTGGAGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTG ACATGCGGATTCGCTGACCTCGGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCC TGCCAAAAGCGTCTGCGGACCCGTCTACTGTGAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCG CCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCCACAGTGTGTGCCAGAGCCCCAAGCCCCTCCC CCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGAATCGTCCCCGCTAAGTCCGTGTG GATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTTAGCATGAGCTATAGCTGGACCGG ATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAG CCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCCGGCCTCGCAAACCGCTAGCAGACAGGCTGAGGTCATC GCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCA ATACCTCGCCGGACTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATG TGCCTGAGTCCGACGCTGCCGCTAGCGCTCACCGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGC GGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCATAGCTCCGTGCTCTGCGAATGCTATGACGC ATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAA TAACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCGCTTGCCAAAGGCAAA AGAAAGTGACAGCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGAC GTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGT ACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCTAGGAAAAAGAGAAACCGTCGTGCTCACC GAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAG ACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTG GCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCATCCCAATATCGAqTTtCATTAC GTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAGTT+TTTACCGAACTGGATGGCGT CCTGAAACTGACACCCATTGCCGCTGCCGGAAGGCTCGACCTCAGCCGATGGTTTACCGCTGGCTATAGCCGGAGGCGATA TCTATCACTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTTGCCGTCCAGACAACTGGCAGAAACTGGCAAGTGTTTTTGG GCTAAGCATATGTGGAACTTTTGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAA AGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAG AGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAGGGGAGAAATTGCGGATAC TGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGGTCAGCTTTAGGGTCG GCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTG AAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAA AGGCAGAGACGCTGTGATTCTGCTCATGTGTGGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTG TGTTTGGCCCTATGCTCACCGATCCCTCCCACATTACCGCTGAGGCTGCCGGAAGGAGCTCGCTAGGGGAAGCCCTCCC TCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGC TGGCCATGCCGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAAGCGGAGCGGAC AATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCATctcgagtgagaattcgcc

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Cassette C

ggoggatccaccatgctogagTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGAT TCTGAATGCCGCTAGCCTCGCCGGAACCCATATCATTCCCGATAGGGAAGTGCTCTACAGGAGACTTTGACGAAATGGAAG AGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACCTCCACCAAAACATTGTGGATGTGCAATAC  $\tt CTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCTAGGTGGTTCTG$ GTTCTGTCTGCTCCTGCCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCCTCGGCTTTG GCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAG GGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGC TAGGAGATTCGCTCAGGCTCTGCCTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTG ACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGC ACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCA AATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCG GCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGTAAGGTCGTGATTCTGGATAGCTTTGACCCTCTGGTCGCC GAAGAGGATGAGAGAGAGAGATTAGCGTCCCCGCTGAGATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCT CACCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGCCTGTGTGTACCAGAGGCGTCG CCAAAGCCGTgGAtTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAATGCCCTCGGC ATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCCCTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGA TATGTCCGCCGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCCGCCTTACTGTC TGTCCACCGGAGCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACC GTGGALTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTCGCGGAGGCCAAATCGTCGGCGG CCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCAC GCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCT GCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACAGTGGTCCTG  ${\tt CGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATCGCCTCA}$ GCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTAC ACAAACGTGGALCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCCTAGCGGAATGTTTGACTCCAGCGTCCTGTG TGAGTGTTACGATGCCGGATGCGCTTGGTATAGGTCCGAGCTCAGCCCTCTGCTCCTCTCCACCACACAGTGGCAGGTCC TGCCTTGCTCCTTCACAACCCTCCCCGCTCTGTCCACCGGACTGAGAAAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGG CATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCTAGCCCTCTGACAACCTCCCAGACACTGCT CTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATtCTCCAGGCTA GCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAAC GGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGG AGAGGTCGCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGAC TCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGAC AGGCATGACCACAGACAATCTGAAATGCCCTCCCGTCGTGCATGGCTGTCCCCTCCCCCAGAAGCCCTCCCGTCC CCCTCCCAGAAAGAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGC TTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGGATACAAAGGCGT  $\tt CTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCATGTGTTTCTGGTCGGCCAAC$ TGTTTACCTTTAGCCCTAGGAGACACTGGACCACACGGGATGCAATTGCTCCATCTTATCCCGGACACATTTTCGTCGGC GCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGG AGACATTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCCAACTGCCTG GAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGG ATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCCTCAGGCTA GGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCC TATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCA ACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTG AGTTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTGCCCCTCTGTAAGCCTCTGCTCAGGGAAACCTGTTAC ATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGAT TATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTC CTCAGCACACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCACAGCCGCTCTGGT CATGGCTCAGCTCCTGAGAATCCCTCAGGCTCCCGGAGCCCTCGTGGTCGCGCTCGTGTGTGCCGCTATCCTCAGGAGAC ACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACACGATAGCCCTGACGCTGAGGCTCATCGAAGCCCAATCTG CTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGTTTACCGGACTGACACACAT TGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGATTTCCCTTACCTCGTGGCTAGGGGAAGGACAGCCTA TCCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTG TTTCCCGATCTGGGAGTGAGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTGCCAAGCTCCCCCTCGCCGTCATGGG GCGCTTACCAACTGGGAAAGGTCCTGGTTGGALATTCTGGCTGGCTATGGCGTTGGCGTCGCCGGAGCCCTCGTGGCTTTC AAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGG **AAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAG** TGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACC CCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCAT TATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTCACCTTTACCATTGAGACAA CCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGGGCAGAACCGGAAGGGGGAAAGCCTGGCATTGACTGTTTC AGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTTGGTgGACTATCCCTA TCTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCTCGTGACACCCTGTGCCGCTTGAGGAACAGA

# 148/216

AACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCT TGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTCAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAA GCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGGCTATAAGGGGAGTGTGGAGGGGAGACGGAAGCG GACCCTGGATCACCACCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATT TTCAAAagatctTGAgtcgacgaattcgcc

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## Melanoma Savine design

Two savines - one containing scrambled melanocyte differentiation Ags
- one containing scrambled melanoma cancer specific Ags

### Genes in melanocyte differentiation Savine

#### m100

MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDCWRGGQVSLKVSNDGPTLI
GANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTW
GQYWQVLGGPVSGLSIGTGRAMLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLR
NQPLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTSCGSSPVPGTTDG
HRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLA
EMSTPEATGMTPAEVSIVVLSGTTAAQVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVK
RQVPLDCVLYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMBISSPGCQPPAQRLCQPVLP
SPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIVGILLVLMAVVLASLIYRRRLMKQD
FSVPOLPHSSSHWLRLPRIFCSCPIGENSPLLSGOOV

#### MART

MPREDAHFIYGYPKKGHGHSYTTAEEAAGIGILTVILGVLLLIGCWYCRRRNGYRALMDKSLHVGTQCALTRRCPQEG FDHRDSKVSLQEKNCEPVVPNAPPAYEKLSAEQSPPPYSP

#### TRP-1

PAFLTWHRYHLLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDICTDDLMGSRSNFDSTLISPNSVFSQWRVVCDSLED YDTLGTLCNSTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPTGKYDPAV RSLHNLAHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVFDEWLRRYNADISTFPLENAPIGHNRQYNMVPFWPPVTNTE MFVTAPDNLGYTYE

### Tyros

MLLAVLYCLLWSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILLSNAPLGPQFPFTGVDDRE SWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTY GQMKNGSTPMFNDINIYDLFVWMHYYVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIP YWDWRDAEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRNPGNHDKSRTPRL PSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHH AFVDSIFEQWLQRHRPLQEVYPEANAPIGHNRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYL EQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLPEEKOPLLMEKEDYHSLYOSHL

### TRP2

MSPLWWGFLLSCLGCKILPGAQGQFPRVCMTVDSLVNKECCPRLGAESANVCGSQQGRQQCTEVRADTRPWSGPYILR NQDDRELWPRKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLSPQEREQFLGALDLAKKRVHPDY VITTQHWLGLLGPNGTQPQFANCSVYDFFVWLHYYSVRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHLLCLERDLQRL IGNESFALPYWNFATGRNECDVCTDQLFGAARPDDPTLISRNSRFSSWETVCDSLDDYNHLVTLCNGTYEGLLRRNQM GRNSMKLPTLKDIRDCLSLQKFDNPPFFQNSTFSFRNALEGFDKADGTLDSQVMSLHNLVHSFLNGTNALPHSAANDP IFVVLHSFTDAIFDEWMKRFNPPADAWPQELAPIGHNRMYNMVPFFPPVTNEELFLTSDQLGYSYAIDLPVSVEETPG WPTTLLVVMGTLVALVGLFVLLAFLQYRRLRKGYTPLMETHLSSKRYTEEA

### MC1R

MAVQGSQRRLLGSLNSTPTAIPQLGLAANQTGARCLEVSISDGLFLSLGLVSLVENALVVATIAKNRNLHSPMYCFIC CLALSDLLVSGTNVLETAVILLLEAGALVARAAVLQQLDNVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIV TLPRAPRAVAAIWVASVVFSTLFIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQG FGLKGAVTLTILLGIFFLCWGPFFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLIYAFHSQBLRRTLKEV LTCSW

## MUC1F

 ${\tt MTPGTQSPFFLLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKNAVSMTSSVLSSHSPGSGSSTTQGQDV\\ {\tt TLAPATEPASGSAATWGQDVTSVPVTRPALGSTTPPAHDVTSAPDNK}$ 

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#### MUC1R

NRPALGSTAPPVHNVTSASGSASGSASTLVHNGTSARATITPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSS VPPLTSSNHSTSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGFLGLSNIKFRPGSV VVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVY LIALAVCQCRKKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTNPAVAAASANL

NB Muc 1 Repeat sequences in the middle of the gene were removed

Genes in melanoma specific Savine

BAGE

MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF

GAGE - 1

 ${\tt MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQGEPQTGCECEDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP$ 

gp100In4

SWSQKRSFVYVWKTWGEGLPSQPIIHTCVYFFLPDHLSFGRPFHLNFCDFL

#### MAGE-1

MSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSE GSSSREEEGPSTSCILESLFRAVITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCFPEIFGKASESLQLVFG IDVKEADPTGHSYVLVTCLGLSYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGE PRKLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRALAETSYVKVLEYVIKVSARVRFFFPSLREAALREEEEGV

#### MAGE-3

MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGEVPAAESPDPPQSPQGASSLPTTMNYP LWSQSYEDSSNQEEEGPSTFPDLESEFQAALSRKVAELVHFLLLKYRAREPVTKAEMLGSVVGNWQYFPPVIFSKASS SLQLVFGIELMEVDPIGHLYIFATCLGLSYDGLLGDNQIMPKAGLLIIVLAIIAREGDCAPEEKIWEELSVLEVFEGR EDSILGDPKKLLTQHFVQENYLEYRQVPGSDPACYEFLWGPRALVETSYVKVLHHMVKISGGPHISYPPLHEWVLREG EE

### PRAME

MERRRLWGSIQSRYISMSVWTSPRRLVELAGQSLLKDEALAIAALELLPRELFPPLFMAAFDGRHSQTLKAMVQAWPF
TCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWKLQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMT
KKRKVDGLSTEAEQPFIPVEVLVDLFLKEGACDELFSYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIKMILKMVQLDS
IEDLEVTCTWKLPTLAKFSPYLGQMINLRRLLLSHIHASSYISPEKEEQYIAQFTSQFLSLQCLQALYVDSLFFLRGR
LDQLLRHVMNPLETLSITNCRLSEGDVMHLSQSPSVSQLSVLSLSGVMLTDVSPEPLQALLERASATLQDLVFDECGI
TDDQLLALLPSLSHCSQLTTLSFYGNSISISALQSLLQHLIGLSNLTHVLYPVPLESYEDIHGTLHLERLAYLHARLR
ELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN

### TRP2IN2

LMETHLSSKRYTEEAGGFFPWLKVYYYRFVIGLRVWQWEVISCKLIKRATTRQP

### NYNSO1a

 ${\tt MQAEGRGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPGGGAPRGPHGGAASGLNGCCRC}\\ {\tt GARGPESRLLEFYLAMPFATPMEAELARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADHRQLQLSISSCLQQLSLLMWITQCFLPVFLAQPPSGQRR}\\$ 

### NYNSO1b

MLMAQEALAFLMAQGAMLAAQERRVPRAAEVPGAQGQQGPRGREEAPRGVRMAARLOG

LAGE1

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MQAEGQGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPRGGAPRGPHGGAASAQDGRCPC GARRPDSRLLQLHITMPFSSPMEABLVRRILSRDAAPLPRPGAVLKDFTVSGNLLFIRLTAADHRQLQLSISSCLQQL SLLMWITQCFLPVFLAQAPSGQRR

```
Differentiation Savine Scramble process
 Disease name
               : melanoma
 Input filename
               : Diffmucg.txt
 Output filename : Diffmucs.txt
 Number genes
               : 8
 Number segments : 187
Segment length : 30
Segment overlap : 15
 Segments in original order:
         : gp100
Segment#
        : 1
Offset
        : 1
1st Codon : 1
 A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R
GCCGCTATGGATCTGGTCCTGAAAAGGTGTCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA
         : gp100
Segment#
        : 2
Offset
        : 16
1st Codon : 1
 V I G A L L A V G 'A T K V P R N Q D W L G V S R Q L R T K A
GTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT
Gene
         : gp100
Segment# : 3
Offset
        : 31
1st Codon : 1
 N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A O R L
AACCAAGACTGGCTGGGAGTGTCCAGGCAACTGAGAACCAAAGCCTGGAACAGCTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC
         : gp100
Gene
Segment#
       : 4
Offset
        : 46
1st Codon : 1
 W N R Q L Y P B W T E A Q R L D C W R G G Q V S L K V S N D
: gp100
Segment# : 5
Offset
        : 61
1st Codon : 1
D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L
GACTGTTGGAGAGGCGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTTAGCATTGCCCTC
Gene
        : gp100
Segment#
       : 6
        : 76
1st Codon : 1
G P T L I G A N A S F S I A L N F P G S Q K V L P D G Q V I
GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGGATGGCCAAGTGATT
Gene
        : gp100
Segment# : 7
Offset
       : 91
1st Codon : 1
N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G
AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA
        : qp100
Segment#
       : 8
Offset
       : 106
1st Codon : 1
```

Figure 27 (Cont)

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```
W V N N T I I N G S Q V W G G Q P V Y P Q B T D D A C I F P
 TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT
         : qp100
  Segment# : 9
  Offset
         : 121
 1st Codon : 1
  Q P V Y P Q B T D D A C I P P D G G P C P S G S W S Q K R S
 CAGCCTGTGTATCCCCAAGAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC
         : qp100
 Segment# : 10
 Offset
         : 136
 1st Codon : 1
  D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L
 GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC
         : qp100
 Segment# : 11
 Offset
        : 151
 1st Codon : 1
 P V Y V W K T W G Q Y W Q V L G G P V S G L S I G T G R A M
 TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG
         : gp100
 Segment# : 12
 Offset
        : 166
 1st Codon : 1
 G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G
 Gene
 Segment# : 13
 Offset
        : 181
 1st Codon : 1
 LGTHTMEVTVYHRRGSRSYVPLAHSSSAFT
 \tt CTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGGGGTCCAGGGTCCTACGTCCCCCTCGCCCATAGCTCCAGCGCTTTCACA
Gene
        : gp100
Segment# : 14
Offset
        : 196
1st Codon : 1
 S R S Y V P L A H S S S A P T I T D Q V P P S V S V S Q L R
AGCAGAAGCTATGTGCCTCTGGCTCACCTCCAGCTCCGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA
Gene
        : qp100
Segment# : 15
Offset
        : 211
1st Codon : 1
 I T D Q V P F S V S V S Q L R A L D G G N K H F L R N Q P L
ATCACAGACCAAGTGCCTTTCTCCGTGTCCGTGTCCCAGCTCAGGGCTCTGGATGGCGGAAACAACACTTTCTGAGAAACCACCCCTC
Gene
        : gp100
Segment# : 16
Offset
        : 226
1st Codon : 1
 A L D G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E
GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAA
Gene
        : gp100
Segment# : 17
Offset
       : 241
1st Codon : 1
 T F A L Q L H D P S G Y L A R A D L S Y T W D F G D S S G T
ACCTTTGCCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA
Gene
       : gp100
Segment# : 18
Offset
       : 256
1st Codon : 1
 A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P
```

# 153/216

Gene : qp100 Segment# : 19 Offset : 271 1st Codon : 1 LISRALVVTHTYLBPGPVTAQVVLQAAIPL CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC Gene : gp100 Segment# : 20 Offset : 286 1st Codon : 1 G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT Gene : gp100 Segment# : 21 Offset : 301 1st Codon : 1 T S C G S S P V P G T T D G H R P T A B A P N T T A G Q V P ACCTCCTGCGGAAGCTCCCCGGTCCCCGGAACCACAGACGGACACAGACCCACAGCCGAAGCCCTAACACAACCGCTGGCCAAGTGCCT Gene : qp100 Segment# : 22 : 316 Offset 1st Codon : 1 R P T A B A P N T T A G Q V P T T B V V G T T P G Q A P T A AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCGCT : gp100 Segment# : 23 Offset : 331 1st Codon : 1 TTEVVGTTPGQAPTABPSGTTSVQVPTTEV ACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGGAACCCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTC Gene : gp100 Segment# : 24 Offset : 346 B P S G T T S V Q V P T T E V I S T A P V Q M P T A E S T G GAGCCTAGCGGAACCACAAGCGTCCCACGCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA Gene : gp100 Segment# : 25 Offset : 361 1st Codon : 1 ISTAPVQMPTAESTGMTPEKVPVSEVMGTT ATCTCCACCGCTCCCGTCCAGATGCCCCACAGCCGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGGAGGTCATGGGAACCACA Gene : qp100 Segment# : 26 Offset : 376 M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCGGCT Gene : gp100 Segment# : 27 Offset : 391 1st Codon : 1 LABMSTPEATGMTPAEVSIVVLSGTTAAQV CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC Gene : gp100 Segment# : 28 Offset : 406 1st Codon : 1 BVSIVVLSGTTAAQVTTTBWVETTARELPI 

Figure 27 (Cont)

Gene

: gp100

# 154/216

Segment# : 29 Offset : 421 1st Codon : 1 T T T B W V B T T A R B L P I P B P B G P D A S S I M S T B ACCACAACCGAATGGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAA Gene : gp100 Segment# : 30 Offset : 436 1st Codon : 1 P B P B G P D A S S I M S T B S I T G S L G P L L D G T A T CCCGAACCCGAAGGCCCTGACGCTAGCTCCATCATGAGCACAGAGTCCATCACAGGCTCCCTGGGACCCCTCCTGGATGGCACAGCCACA Gene : gp100 Segment# : 31 Offset : 451 1st Codon : 1 S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT Gene : gp100 Segment# : 32 Offset : 466 1st Codon : 1 LRLVKRQVPLDCVLYRYGSFSVTLDIVQGI CTGAGACTGGTCAAGAGACAGGTCCCCCTCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT Gene : gp100 Segment# : 33 Offset : 481 1st Codon : 1 RYGSPSVTLDIVQGIESARILQAVPSGEGD AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGGAT : qp100 Segment# : 34 Offset : 496 1st Codon: 1
ESAEILQAVPSGEGDAFELTVSCQGGLPKE CAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA : gp100 Segment# : 35 1st Codon : 1 A F B L T V S C Q G G L P K B A C M B I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAACCCCCTGCCCAA Gene : gp100 Segment# : 36 Offset : 526 A C M B I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V : gp100 Gene Segment# : 37 Offset : 541 1st Codon : 1 R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N AGGCTCTGCCAACCCGTCCTGCCTAGCCCTGCCTGTCAGCTCGTGCTCCACCAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT Gene : gp100 Segment# : 38 Offset : 556 1st Codon : 1 L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T O CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATAGCCAATAGCCTCGCCGTCGTCCCCCAA : gp100 Gene Segment# : 39 Offset : 571

## 155/216

1st Codon : 1 V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L GTGTCCCTGGCTGACAAACTCCCTGGCTGTGGTCAGCACAGGTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC Gene : gp100 Segment# : 40 Offset : 586 1st Codon : 1 LIMPGQBAGLGQVPLIVGILLVLMAVVLAS CTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCGTGCTCGCCTCC Gene Segment# : 41 Offset 1st Codon : 1 I V G I L L V L M A V V L A S L I Y R R R L M K Q D P S V P ATCGTCGGCATTCTGCTCGTCGCTGTGGTCCTGGCTAGCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT : gp100 Gene Segment# : 42 Offset : 616 1st Codon : 1 LIYRRRLMKQDPSVPQLPHSSSHWLRLPRI CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT Gene : gp100 Segment# : 43 : 631 Offset 1st Codon : 1 Q L P H S S S H W L R L P R I F C S C P I G B N S P L L S G CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA Gene : qp100 Segment# : 44 Offset : 646 1st Codon : 1 PCSCPIGENSPLLSGQQVAA TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT : MART Segment# : 1 Offset : 1 1st Codon : 1 A A M P R B D A H F I Y G Y P K K G H G H S Y T T A B E A A GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGACACTCCTACACAACCGCTGAGGAAGCCGCT Gene : MART Segment# : 2 Offset 1st Codon : 1 K K G H G H S Y T T A B B A A G I G I L T V I L G V L L I AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT Gene : MART Segment# : 3 Offset : 31 1st Codon : 1 G I G I L T V I L G V L L L I G C W Y C R R R N G Y R A L M GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCTATAGGGCTCTGATG Gene : MART Segment# : 4 Offset : 46 G C W Y C R R R R G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA Gene : MART Segment# : 5 Offset : 61 1st Codon : 1 D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L

# 156/216

```
GACAAAAGCCTCCACGTCGGCACACGTGTGCCCTCACCAGAAGGTGTCCCCCAAGAGGGGATTCGATCACAGAGACTCCCAAGGTCAGCCTC
        : MART
 Gene
 Segment# : 6
 Offset
        : 76
 1st Codon : 1
 C P Q B G F D H R D S K V S L Q B K N C B P V V P N A P P A
 TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT
        : MART
 Gene
 Segment# : 7
 Offset
        : 91
1st Codon : 1
 Q B K N C B P V V P N A P P A Y B K L S A B Q S P F P Y S P
: MART
Gene
Segment# : 8
Offset
        : 106
1st Codon : 1
 YEKLSABQSPPPYSPAA
TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC
Gene
        : TRP-1
Segment# : 1
Offset
        : 1
1st Codon : 1
 A A P A F L T W H R Y H L L R L B K D M Q B M L Q E P S , P S
GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC
Gene
        : TRP-1
Segment# : 2
Offset
       : 16
1st Codon : 1
 L B K D M Q B M L Q B P S F S L P Y W N F A T G K N V C D I
Gene
        : TRP-1
Segment# : 3
Offset
       : 31
1st Codon : 1
 L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T
CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA
Segment# : 4
Offset
       : 46
1st Codon : 1
C T D D L M G S R S N. P D S T L I S P N S V F S Q W R V V C
TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCGTGTT
        : TRP-1
Gene
Segment# : 5
       : 61
Offset
1st Codon : 1
LISPNSVFSQWRVVCDSLEDYDTLGTLCNS
\tt CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCGTCGGCACACTGTGTAACTCC
Gene
       : TRP-1
Segment# : 6
Offset
      : 76
1st Codon : 1
D S L B D Y D T L G T L C N S T B D G P I R R N P A G N V A
GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT
       : TRP-1
Gene
Segment#
      : 7
1st Codon : 1
T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q
ACCGAAGACCGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCATGGTGCAAAGGCTCCCCGAACCCCCAAGACGTCGCCCAA
```

### 157/216 Gene : TRP-1 Segment# : 8 Offset : 106 1st Codon : 1 R P M V Q R L P B P Q D V A Q C L B V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT : TRP-1 Segment# : 9 Offset : 121 1st Codon : 1 C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P TGCCTCGAGGTCGGCCTCTTCGATACCCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT Segment# : 10 Offset : 136 STNSPRNT V B G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT : TRP-1 Segment# : 11 Offset : 151 1st Codon : 1 T G K Y D P A V R S L H N L A H L P L N G T G G Q T H L S S Gene : TRP-1 Segment# : 12 Offset : 166 H L F L N G T G G Q T H L S S Q D P I F V L L H T P T D A V CACCTCTTCCTCAACGGAACCGGAGGCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTTACCGATGCCGTC : TRP-1 Gene Segment# : 13 Offset : 181 1st Codon : 1 Q D P I P V L L H T F T D A V F D E W L R R Y N A D I S T P CAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT : TRP-1 Segment# : 14 Offset : 196 1st Codon: 1 PDBWLRRYNADISTPPLBNAPIGHNRQYNM PDBWLRRYNADISTPPLBNAPIGHNRQYNM : TRP-1 Segment# : 15 : 211 1st Codon : 1 P L B N A P I G H N R Q Y N M V P F W P P V T N T E M F V T CCCCTCGAGAATGCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA : TRP-1 Gene Segment# : 16 : 226 Offset 1st Codon : 1 V P F W P P V T N T E M F V T A P D N L G Y T Y B A A GTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC Gene : Tyros

Gene : Tyros Segment# : 2

Segment# : 1 Offset : 1 1st Codon : 1

Figure 27 (Cont)

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K
GCCGCTATGCTCCTGGCTGTGCTCTGGTCCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

## 158/216

```
Offset
        : 16
 1st Codon : 1
 Q T S A G H P P R A C V S S K N L M B K E C C P P W S G D R
 Gene
        : Tyros
 Segment# : 3
 Offset
        : 31
1st Codon : 1
 N L M B K B C C P P W S G D R S P C G Q L S G R G S C Q N I
AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAAACTGTCCGGCAGAGGCTCCTGCCAAAACATT
        : Tyros
Segment# : 4
Offset
        : 46
1st Codon : 1
 S P C G Q L S G R G S C Q N I L L S N A P L G P Q P P F T G
AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCTCGGCCCTCAGTTTCCCTTTACCGGA
Gene
Segment# : 5
Offset
1st Codon : 1
 LLSNAPLGPQFPFTGVDDRBSWPSVFYNRT
CTGCTCAGCAATGCCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA
Gene
        : Tyros
Segment# : 6
        : 76
Offset
1st Codon : 1
 V D D R B S W P S V F Y N R T C Q C S G N F M G F N C G N C
GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT
Gene
        : Tyros
Segment# : 7
Offset
       : 91
1st Codon : 1
 C Q C S G N F M G F N C G N C K F G F W G P N C T E R R L L
TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTC
        : Tyros
Segment# : 8
Offset
       : 106
1st Codon : 1
R F G F W G P N C T B R R L L V R R N I F D L S A P B K D K
AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGGCTCCTGGTCAGGAGAAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAAAA
Gene
        : Tyros
Segment# : 9
        : 121
Offset
V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D
GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT
Gene
        : Tyros
Segment# : 10
Offset
      : 136
F F A Y L T L A K H T I S S D Y V I P I G T Y G Q M K N G S
TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC
Gene
       : Tyros
Segment# : 11
Offset
       : 151
1st Codon : 1
Y V I P I G T Y G Q M K N G S T P M P N D I N I Y D L F V W
TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGG
Gene
       : Tyros
Segment# : 12
Offset
      : 166
1st Codon : 1
```

## 159/216

T P M F N D I N I Y D L F V N M H Y Y V S M D A L L G G S E ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA : Tyros Segment# : 13 Offset : 181 1st Codon : 1 M H Y Y V S M D A L L G G S E I W R D I D P A H E A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC Gene : Tyros Segment# : 14 Offset : 196 1st Codon : 1 I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q ATCTGGAGGGATATCGATTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA Gene : Tyros Segment# : 15 Offset : 211 1st Codon : 1 PWHRLFLLRWEQEIQKLTGDENFTIPYWDW CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGCGACTGG : Tyros Segment# : 16 Offset : 226 1st Codon : 1 K L T G D B N F T I P Y W D W R D A B K C D I C T D B Y M G AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA Gene : Tyros Segment# : 17 Offset : 241 1st Codon : 1 RDAEKCDICTDEYMGGQHPTNPNLLSPASF AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT Gene : Tyros Segment# : 18 Offset : 256 1st Codon : 1 G Q H P T N P N L L S P A S P F S S W Q I V C S R L E E Y N GGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT Gene : Tyros Segment# : 19 Offset : 271 1st Codon : 1 FSSWQIVCSRLBEYNSHQSLCNGTPBGPLR TTCTCCAGCTGGCAGATTGTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA Gene : Tyros Segment# : 20 Offset : 286 1st Codon : 1 S H Q S L C N G T P E G P L R R N P G N H D K S R T P R L P AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT Gene : Tyros Segment# : 21 Offset : 301 1st Codon : 1 R N P G N H D K S R T P R L P S S A D V R F C L S L T Q Y E. AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA Gene : Tyros Segment# : 22 Offset : 316 1st Codon : 1 S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGAATTCTGTCTGTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

## 160/216

```
: Tyros
 Segment# : 23
 Offset
         : 331
 1st Codon : 1
  S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S
 AGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC
 Gene
         : Tyros
 Segment# : 24
 Offset
        : 346
 1st Codon : 1
 L E G F A S P L T G I A D A S Q S S M H N A L H I Y M N G T
 CTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA
 Gene
         : Tyros
 Segment# : 25
 Offset
        : 361
 1st Codon : 1
 Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L
 CAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC
 Gene
         : Tyros
 Segment# : 26
 Offset
        : 376
1st Codon : 1
 M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R
ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA
Gene
        : Tyros
Segment# : 27
Offset
        : 391
 H H A F V D S I P B Q W L Q R H R P L Q B V Y P B A N A P I
{\tt CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGAGGCTAACGCTCCCATT}
Gene
        : Tyros
Segment# : 28
Offset
        : 406
1st Codon : 1
 H R P L Q E V Y P B A N A P I G H N R E S Y M V P F I P L Y
CACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCCTTTATCCCTCTGTAT
Gene
        : Tyros
Segment# : 29
Offset
       : 421
1st Codon : 1
G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D
GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT
        : Tyros
Segment# : 30
Offset
       : 436
1st Codon : 1
RNGDFFISSKDLGYDYSYLQDSDPDSFQDY
AGGAATGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTAT
        : Tyros
Segment# : 31
Offset
       : 451
1st Codon : 1
Y S Y L Q D S D P D S F Q D Y I K S Y L B Q A S R I W S W L
TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC
Gene
       : Tyros
Segment# : 32
Offset
       : 466
1st Codon : 1
I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A
Gene
       : Tyros
```

161/216 Segment# : 33 Offset : 481 1st Codon : 1 LGAAMVGAVLTALLAGLVSLLCRHKRKQLP  $\tt CTGGGAGCCGCTATGGTCGGCGGTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT$ : Tyros Segment# : 34 Offset : 496 1st Codon : 1 G L V S L L C R H K R K Q L P B B K Q P L L M B K B D Y H S GGCCTCGTGTCCCTGCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAACAGCCTCTGCTCATGGAAAAGGAAGACTATCACTCC : Tyros Segment# : 35 Offset : 511 1st Codon : 1 E B K Q P L L M B K B D Y H S L Y Q S H L A A GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC : TRP2 Segment# : 1 Offset : 1 1st Codon: 1 AAMSPLWWGFLLSCLGCKILPGAQGQFPRV GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC : TRP2 Gene Segment# : 2 : 16 1st Codon : 1 G C K I L P G A Q G Q P P R V C M T V D S L V N K E C C P R GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA Gene : TRP2 Segment# : 3 Offset : 31 C M T V D S L V N K E C C P R L G A E S A N V C G S Q Q G R Gene : TRP2 Segment# : 4 Offset : 46 1st Codon : 1 LGABSANVCGSQQGRGQCTBVRADTRPWSG CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGAACGCGAACTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA Gene : TRP2 Segment# : 5 Offset : 61 1st Codon : 1 GQCTEVRADTRPWSGPYILRNQDDRELWPR GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA : TRP2 Segment# : 6 Offset : 76 PYILRNQDDRELWPRKFFHRTCKCTGNFAG CCCTATATCCTCAGGAATCAGGATGACAGAGAGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA : TRP2 Segment# : 7 Offset : 91 1st Codon : 1

AAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGGATTGCAAATTCGGATGGACAGGCCCTAACTGT : TRP2 Segment# : 8 Offset

: 106

Figure 27 (Cont)

K P P H R T C K C T G N F A G Y N C G D C K F G W T G P N C

## 162/216

1st Codon : 1 Y N C G D C K P G W T G P N C B R K K P P V I R Q N I H S L Gene : TRP2 Segment# : 9 1st Codon : 1 BRKKPPVIRQNIHSLSPQEREQFLGALDLA Gene : TRP2 Segment# : 10 Offset : 136 1st Codon : 1 SPQBREQFLGALDLAKKRVHPDYVITTQHW AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG Gene : TRP2 Segment# : 11 : 151 Offset 1st Codon : 1 K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q P A N AAGAAAAGGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT Gene : TRP2 Segment# : 12 Offset : 166 1st Codon : 1 LGLLGPNGTQPQFANCSVYDFPVWLHYYSV CTGGGACTGCTCGGCCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC Gene : TRP2 Segment# : 13 Offset : 181 C S V Y D F F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT Segment# : 14 Offset : 196 1st Codon : 1 RDTLLGPGRPYRAIDFSHQGPAFVTWHRYH AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT Gene : TRP2 Segment# : 15 Offset : 211 1st Codon : 1 FSHQGPAFVTWHRYHLLCLERDLQRLIGNE TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA : TRP2 Gene Segment# : 16 Offset : 226 1st Codon : 1 L L C L B R D L Q R L I G N B S F A L P Y W N F A T G R N R CTGCTCTGCCTCGAGAGAGCCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAA : TRP2 Gene Segment# : 17 Offset 1st Codon : 1 S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D : TRP2 Gene Segment# : 18 Offset : 256 1st Codon : 1 C D V C T D Q L P G A A R P D D P T L I S R N S R F S S W R

## 163/216

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TGCGATGTGTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA
        : TRP2
 Gene
 Segment# : 19
 Offset
        : 271
 1st Codon : 1
  D P T L I S R N S R P S S W E T V C D S L D D Y N H L V T L
 GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC
 Gene
        : TRP2
 Segment# : 20
        : 286
 Offset
 1st Codon : 1
 TVCDSLDDYNHLVTLCNGTYEGLLRRNQMG
 ACCUTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGA
 Gene
        : TRP2
 Segment# : 21
 Offset
 1st Codon : 1
 C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C
TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT
Gene
        : TRP2
Segment# : 22
Offset
       : 316
1st Codon : 1
 R N S M K L P T L K D I R D C L S L Q K F D N P P P P O N S
Gene
       : TRP2
Segment# : 23
Offset
       : 331
1st Codon : 1
 LSLQKFDNPPPPQNSTFSFRNALEGFDKAD
CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT
Gene
Segment# : 24
Offset
       : 346
1st Codon : 1
 T F S F R N A L E G F D K A D G T L D S Q V M S L H N L V H
ACCITTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT
Gene
       : TRP2
Segment# : 25
Offset
       : 361
G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N
Gene
       : TRP2
Segment# : 26
Offset
       : 376
1st Codon : 1
S F L N G T N A L P H S A A N D P I F V V L H S F T D A I P
AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTCGTCCACTCCTTCACAGACGCTATCTTT
       : TRP2
Gene
Segment# : 27
Offset
       : 391
1st Codon : 1
D P I F V V L H S F T D A I F D E W M K R F N P P A D A W P
GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT
       : TRP2
Gene
Segment# : 28
       : 406
Offset
1st Codon : 1
D B W M K R P N P P A D A W P Q E L A P I G H N R M Y N M V
GACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC
```

## 164/216

Gene : TRP2 Segment# : 29 Offset : 421 1st Codon : 1 Q B L A P I G H N R M Y N M V P F P P V T N B B L P L T S : TRP2 Segment# : 30 Offset : 436 1st Codon : 1 P F F P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V CCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC : TRP2 Segment# : 31 Offset : 451 1st Codon : 1 DQLGYSYAIDLPVSVEETPGWPTTLLVVMG GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA : TRP2 Segment# : 32 Offset : 466 1st Codon : 1 BETPGWPTTLLVVMGTLVALVGLPVLLAFL GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTCGTCGTCACTGCTCGCCCCTCGTGGCACTGTTTGTGCTCCTGGCTTTCCTC Gene : TRP2 Segment# : 33 Offset : 481 1st Codon : 1 T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTTATACCCCTCTGATGGAGACA : TRP2 Gene Segment# : 34 : 496 Offset 1st Codon : 1 Q Y R R L R K G Y T P L M E T H L S S K R Y T B B A A A CAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCATCTGTCCAGCAAAAAGGTATACCGAAGAGGCTGCCGCT Gene Segment# : 1 Offset A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCCTCGCCGCT Gene : MC1R Segment# : 2 Offset : 16 LNSTPTAIPQLGLAANQTGARCLEVSISDG  $\tt CTGAATAGCACCCCACAGCCATTCCCCCAACTGGGACTGGCTGCCCAATCAGACAGGCGCTTAGGTGTCTGGAAGTGTCCATCTCCGACGGA$ : MC1R Gene Segment# : 3 Offset : 31 1st Codon : 1 N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTC Gene : MClR Segment# : 4 Offset 1st Codon : 1 L F L S L G L V S L V E N A L V V A T I A K N R N L H S P M CTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG Gene : MC1R Segment# : 5

## 165/216

Offset : 61 1st Codon : 1 V V A T I A K N R N L H S P M Y C P I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCCCCTCAGCGATCTGCTCGTGTCC Gene : MC1R Segment# : 6 Offset : 76 1st Codon : 1 Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A TACTGTTTCATTTGCTGTCGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT Gene : MC1R Segment# : 7 Offset : 91 1st Codon : 1 G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT Gene : MC1R Segment# : 8 Offset : 106 1st Codon : 1 G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGATGTATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT : MC1R Gene Segment# : 9 Offset : 121 1st Codon : 1 V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT Gene Segment# : 10 Offset : 136 1st Codon : 1 F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA : MC1R Gene Segment# : 11 Offset : 151 1st Codon : 1 A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC : MC1R Gene Segment# : 12 Offset : 166 1st Codon : 1 A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V GCCGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTC : MC1R Gene Segment# : 13 Offset : 181 1st Codon : 1 FIAYYDHVAVLLCLVVFFLAMLVLMAVLYV TTCATTGCCTATTACGATCACGTCGCCGTCCTGCTCTCGTCGTCTTCTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTC : MC1R Gene Segment# : 14 : 196 Offset 1st Codon : 1 V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA : MClR Gene Segment# : 15 Offset : 211 1st Codon : 1

# 166/216

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATECTEGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCAAAGGCCTGTGCATCAGGGATTCGGACTGAAA : MC1R Gene Segment# : 16 Offset : 226 1st Codon : 1 LHKRQRPVHQGPGLKGAVTLTILLGIPFLC Gene : MC1R Segment# : 17 Offset : 241 1st Codon : 1 G A V T L T I L L G I F F L C W G P F P L H L T L I V L C P GCCCTGTGACACTGACAATCCTCCTGGGAATCTTTTTCCTCTGCTGGGGCCCCTTTCTTCTGCATCTGACACTGATTGTGCTCTGCCCT Gene : MC1R Segment# : 18 Offset : 256 1st Codon : 1 W G P F F L H L T L I V L C P B H P T C G C I P K N F N L F TGGGGACCCTTTTCCTCCACCTCACCCTCATCGTCCTGTGTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT Gene : MC1R Segment# : 19 Offset : 271 1st Codon : 1 B H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATTTTGCAATGCCATTATCGATCCCCTCATCTAT Segment# : 20 Offset : 286 1st Codon : 1 LALIICNAIIDPLIXAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC Gene : MC1R Segment# : 21 Offset : 301 1st Codon : 1 AFHSQELRRTLKEVLTCSWAA GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC : MUCLP Gene Segment# : 1 Offset A A M T P G T Q S P F F L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC Gene : MUC1F Segment# : 2 Offset : 16 L L T V L T V V T G S G H A S S T P G G E K E T S A T Q R S CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGAAAGAGACAAGCGCTACCCAAAGGTCC : MUC1F Gene Segment# : 3 : 31 Offset 1st Codon : 1 STPGGEKETSATQRSSVPSSTEKNAVSMTS AGCACACCGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCC : MUC1F Gene Segment# : 4 : 46 Offset 1st Codon : 1 S V P S S T B K N A V S M T S S V L S S H S P G S G S S T T AGCSTCCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCCCCGGGAAGCGGAAGCTCCACCACA

## 167/216

: MUC1P Segment# : 5 Offset : 61 1st Codon : 1 S V L S S H S P G S G S S T T Q G Q D V T L A P A T E P A S Gene : MUC1F Segment# : 6 : 76 Offset 1st Codon : 1 Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGGCTCCCGCTACCGGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC : MUC1F Gene Segment# : 7 Offset : 91 1st Codon : 1 G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V GGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGTGCCTGTGACAAGGCCTGCCCTCGGCTCCACCACACCCCCTGCCCATGACGTC Gene : MUC1F Segment# : 8 Offset : 106 1st Codon : 1 TRPALGSTTPPAHDVTSAPDNKAA ACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT : MUC1R Segment# : 1 1st Codon : 1 A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAGCACA Gene : MUC1R Segment# : 2 Offset : 16 1st Codon : 1 N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A AACGTCACCTCCGCCTCCGGCTCCGGCTCCGCCTCCGCCTCCACCCTCGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCGCCT : MUC1R Gene Segment# : 3 Offset : 31 1st Codon : 1 L V H N G T S A R A T T T P A S K S T P P S I P S H H S D T CTGGTCCACAATGGCACAAGGGCTAGGGCTACCACAACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA Gene : MUC1R Segment# : 4 Offset : 46 1st Codon: 1
SKSTPFSIPSHHSDTPTTLASHSTKTDASS
SKSTPFSIPSHHSDTPTTLASHSTKTDASS Segment# : 5 Offset : 61 1st Codon : 1 PTTLASHSTKTDASSTHHSSVPPLTSSNHS CCCACAACCCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACCACTAGCTCCGTGCCTCCCCTCACCTCCAGCAATCACTCC : MUC1R Segment# : 6 Offset. : 76 1st Codon : 1 THH SSV PPLTSSN H STSPQLSTG V SFFFLS Gene : MUC1R

168/216 Segment# : 7 Offset : 91 1st Codon : 1 T S P Q L S T G V S F F F L S P H I S N L Q P N S S L B D P ACCTCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT : MUC1R Gene Segment# : 8 Offset : 106 1st Codon : 1 FHISNLQFNSSLEDPSTDYYQELQRDISEM TTCCATATCTCCAACCTCCAGTTTAACTCCAGCCTCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATG : MUC1R Gene Segment# : 9 Offset : 121 1st Codon : 1 STDYYQELQRDISEMPLQIYKQGGFLGLSN AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT : MUC1R Gene Segment# : 10 Offset : 136 1st Codon : 1 PLQIYKQGG FLGLSNIK FRPG/SVVVQLTLA TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCT : MUC1R Gene Segment# : 11 Offset : 151 1st Codon: 1 IK P R P G S V V V Q L T L A F R B G T I N V H D V B T Q F : MUC1R Segment# : 12 Offset : 166 1st Codon : 1 FREGTINVHDVETQFNQYKTRAASRYNLTI TTCAGAGAGCGAACCATTAACGTCCACGATGTGGAAACCCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT : MUC1R Gene Segment# : 13 Offset : 181 1st Codon : 1 N Q Y K T B A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA : MUC1R Gene Segment# : 14 Offset : 196 1st Codon : 1 S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTGTCCGTGTCCGACGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGCTGGCGCTCCCCGGATGGGGAATCGCTCTGCTCCTGCTC Gene : MUC1R Segment# : 15 Offset : 211 1st Codon: 1 S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGCGGGCATTGCCCTCCTGGTCTGGTCTGGTCCTGGTCCTGGTCGCCATTGTGTATCTGATTGCCCTC Gene : MUC1R Segment# : 16 Offset : 226 1st Codon : 1 V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I 

Gene : MUC1R Segment# : 17 Offset : 241

Figure 27 (Cont)

## 169/216

1st Codon : 1

A V C Q C R R K N Y G Q L D I F P A R D T Y H P M S B Y P T GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

Gene : MUC1R
Segment# : 18
Offset : 256
1st Codon : 1

Gene : MUC1R Segment# : 19 Offset : 271 1st Codon : 1

Y H T H G R Y V P P S S T D R S P Y E K V S A G N G G S S L
TACCATACCCATGGCAGATACGTCCCCCTAGGCTCCACCGATAGGTCCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

Gene : MUC1R Segment# : 20 Offset : 286 1st Codon : 1

S P Y B K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGGCGCAATCTGGCT

Gene : MUC1R
Segment# : 21
Offset : 301
1st Codon : 1

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

Segments in scrambled order:

-----

gp100 #4

W N R Q L Y P E W T E A Q R L D C W R G G Q V S L K V S N D
TGGAATAGGCAACTGTATCCCGAATGGACAGAGCTCAGAGACTGGATGCTGGAGGGCGAGGCCAAGTGTCCCTGAAAGTGTCCAACGAT

TRP2 #6

Tyros #30

RNGDFFISSKDLGYDYSYLQDSDPDSFQDY AGGAATGCCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATTAGCTATTCTGCAAGACTCCGACCCTGACCCTTCCAAGACTAT

TRP-1 #1

A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S F S GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC

Tyros #29

G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT

TRP2 #16

LLCLBRDLQRLIGNBSFALPYWNFATGRNECTGCTCTGCCTCGCAGAGAGACGAAACGAA

gp100 #23

MUC1R #9

gp100 #36

A C M B I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V GCCTGTATGGAAATCTCCAGCCTGGCTGCCAGCCTCCGGCTCAGAGACTGTGTCAGCCTGTCCTCCCCCCGCTTGCCAACTGGTC

TRP2 #31

D Q L G Y S Y A I D L P V · S V E E T P C W P T T L L V V M G

## 170/216

GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA

TRP-1 #7

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCCATTAGGAGAAACCCTGCCGGAAACGTCGCCCAGACCCCATGGTGCAAAGGCTCCCCGAACCCCCAAGACGTCGCCCAA

TRP2 #3

C M T V D S L V N K E C C P R L G A E S A N V C G S Q Q G R TGCATGACCGTCGGCTCAGCATGTCTCGCCAGCAAGGCAGA

MUC1R #13

N Q Y K T B A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTCGCACATCTCGCGCCAA

TRP2 #1

A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V GCCGCTATGTCCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC

gp100 #18

qp100 #27

LABMSTPBATGMTPABVSIVVLSGTTAAQV
CTGGCTGAGATGAGCACACCGAAGCCACAGGCATGACCCCTCCGGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC

MUC1R #11

MUCLF #7

G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V GGCTCCGCCCTACCTCGCCCACACCCCCCTGCCCATGACGTC

MC1R #16

MCIR #20

LALIICNAIIDPLIYAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC

TRP2 #

K F P H R T C K C T G N F A G Y N C G D C K F G W T G P N C AAGTTTTTCCATAGGACAGGAAATTCGGAAATTCGGATGGACAGGCCCTAACTGT

TRP2 #23

L S L Q K F D N P P F F Q N S T F S F R N A L E G F D K A D CTGTCCCTGCAAAGTTTGACAATCCCCTTTCTTTCAGAATAGCACATCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT

MUCIR #4

MUCIR #1

A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGACCCCTCTCGGAAGCACCACCAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAGCACAA

TRP2 #21

C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGCAGAAACTCCATGAAACTGCCTCAAGGATATCAGAGACTGT

MIIC112 #4

MC1R #13

FIAYYDHVAVLLCLVVFFLAMLVLMAVLYV

Tyros #16

K L T G D R N F T I P Y W D W R D A E K C D I C T D E Y M G

## 171/216

AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA

gp100 #32

L R L V K R Q V P L D C V L Y R Y G S F S V T L D I V Q G I CTGAGACTGGTCAAGAGACAGGTCCCCCTCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT

MUCLR #10

F L Q I Y K Q G G F L G L S N I K F R P G S V V V Q L T L A TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGACCTGACACTGGCT

MC1R #9

Tyros #21

RNPGNHDKSRTPRLPSSADVBFCLSLTQYBAGGAAACCCAAAAAGCAGAAACCCAAAAAGCAGAAACCCCTAGGCTCCCCTCCAGCGCTGACGTTTTGCCTCAGCCTCACCCAATACGAA

TRP-1 #14

F D E W L R R Y N A D I S T F P L E N A P I G H N R Q Y N M TTCGATGAGTGGCTGGAAAGGCTATAACAGTATAACATG

gp100 #39

V S L A D T N S L A V V S T Q L I M P G Q B A G L G Q V P L GTGTCCCTGGCTGACACAACTCCCTGGCTGGTCAGCACACACCTCATCATCCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC

gp100 #20

G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H
GGCCCTGTGACAGCCCAAGTGGTCCTGCAGAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT

Tyros #8

K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K AAGTITGGCTTTTGGGGACCCAATTGCACGAGAGAGAGACGCTCCTGGTCAGGAGAACCATTTTCGATCTGTCCCCCCCTGAGAAAGACAAA

qp100 #13

L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A F T CTGGGAACCCATACCATGGAGGTCACCATACCATAGGAGGTCCAGGGCTTTCACA

MCLR #12

TRP2 #25

G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N GGCACACTGGATAGCCAAGTGACGAACCAATCTGGTCCACTCCTCCACAGCGAACCAATGCCCTCCCCCATAGCGCTGCCAAT

MART #4

G C W Y C R R R N G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA

Tyros #15

PWHRLFLLRWEQEIQKLTGDENFTIPYWDW

MClR #1

A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGGCTCCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCT

MCID #5

V V A T I A K N R N L H S P N Y C F I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTTGTCC

Tyros #25

Tyros #18

G Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N
GGCCAACACCCTACCAATCCCAATCTGCTCAGCCTCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT

MC1R #6

Y C P I C C L A L S D L L V S G T N V L E T A V I L L E A

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TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCCGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT

TRP2 #19

D P T L I S R N S R F S S W E T V C D S L D D Y N H L V T L GACCCTCACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGGACTCCCTGGATGACTATAACCATCTGGTCACCCTC

NUCLE #6

TRPALGSTTPPAHDVTSAPDNKAA
ACCAGACCCGCTCTGGGAAGCAGCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT

Tyros #17

R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F AGGGATGCCGAAAAGTGTGCACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAAACCCTAACCTCCCCCGCTAGCTTT

qp100 #17

T F A L Q L H D P S G Y L A E A D L S Y T W D F G D S S G T ACCTITECCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGACGCTGACCTCCAGCTATACCTGGGGACTTTGGCGATAGCTCCGGCACA

Tyros #22

S S A D V B F C L S L T Q Y B S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGATTCTCTTCTTCTCTCAGAAACACA

qp100 #6

G P T L I G A N A S P S I A L N F P G S Q K V L P D G Q V I GGCCCTACCCTCATCGGGCCAATGCCTCCTCCATCGCTCTCGATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT

MC1R #18

W G P F F L H L T L I V L C P E H P T C G C I F K N F N L P TGGGGACCCTTATCTCATCCTCATCGTCTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT

Tyros #7

CQCSGNFMGFNCGNCKFGFWGPNCTBRRLLTGCCAATGCTCCGGCCATTCTGGGCCATTCTGGGCAATTCCAAATTCGGATTCTGGGCCCTAACTGTACCGAAAGGAGACTGCTC

TRP2 #34

QYRRLRKGYTPLMETHLSSKRYTEEAAACCCGTGGGAAAAGGTATACCGAAGAGGCTGCCGCT

TRP-1 #15

PLENAPIGHNRQYNMVPFWPPVTNTEMFVTCCCCTCGGGGAATGCCCCTATCGGACACAATAGGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA

gp100 #7

N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G AACTITCCCGGAAGGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA

gp100 #22

RPTABAPNTTAGQVPTTEVVGTTPGQAPTA

MUCLE #3

S T P G G E K E T S A T Q R S S V P S S T E K N A V S M T S AGCACACCGGAGGCGGAAAAGGAAACCTCCGCCCACAGAGAAGCTCCGCCTCACCGAAAAGAATGCCGTCAGCATCACCTCC

qp100 #42

LIYRRRLMKQDPSVPQLPHSSSHWLRLPRI CTGATTTACAGAAGGAGACTGATGAGCAAGACTTTAGCGTCCCCAACTGCCTCAGCTCCCACTGCCTCACTCCCACTGCCTCAGCACTGCCTAGGATT

TPD2 #12

L G L L G P N G T Q P Q F A N C S V Y D F F V W L H Y Y S V CTGGGACTGCTCACGCACCCCAACCCCAACTCGCTAACGGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC

TRP-1 #9

C L E V G L P D T P P F Y S N S T N S F R N T V B G Y S D P
TGCCTCGAGGCTCTTCGATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT

ap100 #1

A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R GCCGCTATGGATCTGGTTCTGAAAAGGTCCCCCAGAGAGCCCTCCTCGCTGTCGGAGCCCCCAGAGAGGTCCCCCAGA

MC1R #3

NQTGARCLEVSISDGLFLSLGLVSLVENAL

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 ${\tt AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGAGAATGCCCTC}$ 

Tyros #23

S G S M D K A A N F S P R N T L B G F A S P L T G I A D A S AGGGGAAGCATGGCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC

Tyros #4

SPCGQLSGRGSCQNILLSNAPLGPQFPFTG

Tyros #13

M H Y Y V S M D A L L G G S B I W R D I D F A H B A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC

Tyros #35

TRP2 #5

GQCTEVRADTRPWSGPYILRNQDDRBLWPR GGCCAATGCACAGAGGTCAGGGCTGACACAGAGGCCTTAGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA

MUC1F #4

Tyros #12

T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E ACCCCTATGITTACGATATCAATATCTATGACCTCTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA

gp100 #9

Q P V Y P Q E T D D A C I P P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCGGCTCCTGGTCCCAGAAAAGGTCC

TRP-1 #6

D S L B D Y D T L G T L C N S T E D G P I R R N P A G N V A GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT

qp100 #8

W V N N T I I N G S Q V W G G Q P V Y P Q B T D D A C I F P
TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT

MART #7

cm100 #14

SRSYVPLAHSSSAFTITDQVPFSV5V5QLR AGCAGAAGCTATGTGCCTCTGGCTCAGCTCCAGCTCAGCCTTTACCATTACCGTCAGGTCCCCCTTTAGCGTCAGCGTCAGCCTAACTGAGA

TRP-1 #:

LEKDMQEMLQEPSFSLPYWNFATGKNVCDICTGGAAAAGGATATGCAAGAGATGTGTGGACATT

TPD-1 #16

V P F W P P V T N T E M F V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC

TRP2 #13

C S V Y D P F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCTCTGGCTCACTATTACTCCGTGAGAGACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT

Tvros #9

VRRNIFDLSAPEKDKFFAYLTLAKHTISSD GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT

MART #2

K K G H G H S Y T T A E E A A G I G I L T V I L G V L L I AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT

gp100 #11

PVYVWK.TWGQYWQVLGGPVSGLSIGTGRAM

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TTCGTCTACGTCTGGAAAACCTGGGGCCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG

gp100 #12

ap100 #25

Tyros #19

PSSWQIVCSRLEBYNSHQSLCNGTPEGPLRTTCTCCAGCTGCAGATTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA

TRP2 #27

DPIPVVLHSFTDAIPDEWMKRFNPPADAWPGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGTTGCCTTTCGATGAGTGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT

MC1R #15

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTTGGCATGACACGCTCAGGGAATCGCTGGGCTCCACAAAAGGCCAAGGCCTGTGCATCAGGGATTCGGACTGAAA

MUCLF #2

L L T V L T V V T G S G H A S S T P G G E K B T S A T Q R S CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGCACACGCTAGCTCCACCCCTGGCGGAGAAAAGAGACAAGCGCTACCCAAAGGTCC

gp100 #44

F C S C P I G B N S P L L S G Q Q V A A
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT

TRP2 #24

T F S F R N A L E G F D K A D G T L D S Q V M S L H N L V H ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Tyros #20

SHQSLCNGTPEGPLRRNPGNHDKSRTPRLPAGCCATCAGTCCCTGTGAACGCCCTGAGGGCACCCCTGAGGAGAACCCCTGGGGAACCCCTGGGGAACCCCTGAGGACACCCAGACTGCCT

TRP2 #30

PFFPPVTNEBLFLTSDQLGYSYAIDLPVSVCCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC

TPP2 #9

TRP2 #29

gp100 #28

MUCLR #7

T S P Q L S T G V S F F F L S F H I S N L Q F N S S L K D P ACCTCCCCCAACTGTCCACCGGGGGGTGTCCTTCTTTTTCCTCAGCTTTCACATTGGCAACTCTGCAATTCAATAGCTCCCTGGAAGACCCT

MUC1R #19

YHTHGRYVPPSSTDRSPYBKVSAGNGGSSL TACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

MC1D #4

LPLSLGLVSLVENALVVATIAKNRNLHSPMCTGTTTTCTGTCCCTGGGATAGCTCGTCGTGGAAAACGCTCTGGTCGTGGTGCTGCCATGCCAAAAACAGAAACCTCCACTCCCCCATG

TRP2 #26

S F L N G T N A L P H S A A N D P I F V V L H S F T D A I P
AGCITTCTGAATGGCACAAACGCTCTCCCTCACTCCCCCCCCTAACGATCCCATTTTCGTCGTCCTCCACTCCTTCACAGACGCTATCTTT

WC1R #17

AVCQCRRKNYGQLDIFPARDTYHPMSEYPT

## 175/216

GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGGATACCTATCACCCTATGTCCGAGTATCCCACA

MC1R #14

V P P L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGTCTGATGGCCGTCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA

TRP-1 #10

S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGGGTTCCCACAGGCAAATCCGGTTGAGAAGCCTCCACAATCTGGCT

TRP-1 #3

LPYWNFATGKNVCDICTDDLMGSRSNFDST CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAGCAATTTCGATAGCACA

gp100 #15

MUCLR #8'

FRISNLQFNSSLEDPSTDYYQELQRDISEM
TTCCATATCTCCAACCTCCAGCTTAACTCCAGCCTCGAGGATCCCTCCACCGATTACTATCTACGGAACTGCAAAGGGATATCTCCGAGGATG

MUC1R #20

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGCCGCATCTGGCTACCAAAACCCTGCCGTCGCCGCCGCCCAATCTGGCT

Tyros #11

Y V I P I G T Y G Q M K N G S T P M P N D I N I Y D L P V W
TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACACCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGGG

gp100 #37

R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N
AGGCTCTGCCAACCCGTCCTGCCTGCCTGCCTGCTCAGCTCGTCCACAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT

cm100 #33

RYGSFSVTLDIVQGIESAEILQAVPSGEGD AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGGGAT

Tyros #27

H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTTACCCTGAGGCTAACGCTCCCATT

TRP-1 #4

MUC1R #18

NUC1R #21

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGGCTGCCGCTAGCGCTAACCTCGCCGCT

MC1R #19

E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGATGCATTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCTATTTGCAATGCCATTATCGATCCCTCATCTAT

Tyros #26

MSQVQGSANDPIFLLHHAFVDSIFEQWLQR ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA

TPP2 #22

qp100 #19

LISRALVVTHTYLEPGPVTAQVVLQAAIPL CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACGCTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC

TRP2 #17

S P A L P Y W N P A T G R N B C D V C T D Q L F G A A R P D

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gp100 #:

VIGALLAVGATKVPRNQDWLGVSRQLRTKA GTGATTGGCGCTCTGCCGCGCTCGGCGCTCAGAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT

gp100 #16

A L D G G N K H P L R N Q P L T F A L Q L H D P S G Y L A E GCCCTCGACGGAGGCAATAAGCATTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCTTGACGTACCGCAGAA

TRP2 #18

C D V C T D Q L F G A A R P D D P T L I S R N S R F S S W E TGCGATGTGTGTACCGATCAGGTCTTCGGAGCCGCTTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA

MART #1

A A M P R B D A H P I Y G Y P K K G H G H S Y T T A B B A A GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATCGCTATCCCAAAAAGGGACACTCCTACACAACCGCTGAGGAAGCCGCT

TRP-1 #11

MUC1R #14

S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTCCGTGTCCGTGTCCCTTTTCCCTTTTAGCGCTCAGTCCGGGGGCTCGCGGTCCCCGGATGGGGAATCGCTCTGCTCGTGCTC

TRP2 #10

SPQEREQFLGALDLAKKRVHPDYVITTQHW AGCCCTCAGGAAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG

Tyros #10

F F A Y L T L A K H T I S S D Y V I P I G T Y G Q M K N G S TTCTTTGCCTATCTGACACTGGCACAGATGAGAATGGCTCC

MC1R #7

G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N
GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCCGTGGCTTAGGGCTGCCGTCCTGCAACAGCTCCAACAAT

MUC1R #16

MART #6

C P Q B G P D H R D S K V S L Q B K N C E P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT

MUC1F #5

S V L S S H S P G S G S S T T Q G Q D V T L A P A T B P A S AGCGTCCTGTCCAGCCTTGGCTCCAGGGCTCCAGGCCCAAGGCCTAGGCCTCGCCCTTGCCCCTTGCCACAGAGCCTTGCCTCC

TRP2 #28

D B W M K R F N P P A D A N P Q B L A P I G H N R M Y N M V GACGAATGGATGAAGAGATTCAATCCCCTGCCGATGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC

MC1R #21

A F H S Q E L R R T L K E V L T C S W A A GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC

TRP2 #15

TRP-1 #8

RPMVQRLPEPQDVAQCLEVGLPDTPPPYSN AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT

TRP-1 #13

Q D P I F V L L H T F T D A V P D E W L R R Y N A D I S T F CAGGATCCCATTTTCGTCCTCCTCACACACTTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

TRP2 #4

 $\begin{smallmatrix} L & G & A & E & S & A & N & V & C & G & S & Q & Q & G & R & G & Q & C & T & E & V & R & A & D & T & R & P & W & S & G \\ \end{smallmatrix}$ 

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CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA

TRP2 #8

TRP-1 #12

H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V CACCTCTTCCTCAACGGAACCCGAACCCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Tyros #34

G L V S L L C R H K R K Q L P B B K Q P L L M B K B D Y H S GGCCTCGTGTCCCTGAGAGACAAAAGGAAACAGCTCCCCGAAGAGAAAAGGCTCCCCGAAAAGGAAAAGGAAAACGCTCCCCGAAGAGAAAAGGAAAAAGGAAAACAGCTCCCCGAAGAGAAAAGGAAAAAGGAAAACAGCTCCCCGAAGAGAAAAGGAAAAAGGAAGACTATCACTCC

TRP2 #2

G C K I L P G A Q G Q P P R V C M T V D S L V N K B C C P R GGCTGTAAGATTCTGCCTGGGGCTCAGGGAATGCTGTCCCAGA

gp100 #43

Q L P H S S S H N L R L P R I P C S C P I G E N S P L L S G CAGCTCCCCCATAGCTCCAGCCATAGCCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA

gp100 #10

D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAAGCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC

gp100 #3

N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L AACCAAGACTGGCTGGGGGGCTGGGGAGCCCAAAGGCTC

Tyros #14

I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q ATCTGGAGGGATATCGATTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACACGAAATCCAA

MUC1F #1

A A M T P G T Q S P P P L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCCAAAGCCCTTTCTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC

MART #5

DKSLHVGTQCALTTRRCPQEGFDHRDSKVSLGACAAAAGCCTCCACGGCACACAGTGTGCCCTCACCAGAAGGTGTCCCCAAGAGGGTTCGATCACAGAGACTCCAAGGTCAGCCTC

MUCLR #2

N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A AACGTCACCTCCGCCTCCGCCTCCGCCTCCACCCTCCGCAACCTCCGCCAGAGCCACAACCACCACCCCGCT

Tyros #24

L B G F A S P L T G I A D A S Q S S M H N A L H I Y M N G T CTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA

TRP2 #14

R D T L L G P G R P Y R A Y D F S H Q G P A F V T W H R Y H AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT

Tyros #1

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K GCCGCTATGCTCCTGGCTGTGCTCTGGTCCTGGCCAGACCTCCGCCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

gp100 #35

A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTGCAGGGGGCCCTCCCCAAAGAGGGCTTGCATGGAGATTAGCTCCCCGGATGCCAACCCCCTGCCCAA

Tyros #6

V D D R B S W P S V F Y N R T C Q C S G N F M G F N C G N C GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT

gp100 #34

ESAEILQAVPSGEGDAFELTVSCQGGLPKEGAGAGGGAGAGGCGTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA

TRP2 #20

T V C D S L D D Y N H L V T L C N G T Y E G L L R R N Q M G

## 178/216

ACCGTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGA

L L S N A P L G P Q F P F T G V D D R B S W P S V F Y N R T CTGCTCAGCAATGCCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA

YEKLSABQSPPPYSPAA TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC

gp100 #41

Î V G I L L V L M A V V L A S L I Y R R R L M K Q D F S V P ATOGTOGGCATTCTGCTCGTGCTCATGGCTGTGGTCCTGGCTAGCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTCTCCGTGCCT

G I G I L T V I L G V L L L I G C W Y C R R R N G Y R A L M GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTCCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCTATAGGGCTCTGATG

Tyros #31
Y S Y L Q D S D P D S F Q D Y I K S Y L E Q A S R I W S W L TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC

Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC

T S C G S S P V P G T T D G H R P T A B A P N T T A G O V P ACCTCCTGCGGAAGCTCCCCCGTCCCCGGAACCACAGACGGACACAGACCCACAGGCCGAAGCCCCTAACACAACCGCTGGCCAAGTGCCT

LVHNGTSARATTTPASKSTPFSIPSHHSDT CTGGTCCACAATGGCACAAGCGCTAGGGCTACCACACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA

E B T P G W P T T L L V V M G T L V A L V G L F V L L A P L GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTC

gp100 #29

T T T E N V E T T A R E L P I P E P E G P D A S S I M S T E ACCACAACCGAATGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAA

G A V T L T I L L G I P P L C W G P F P L H L T L I V L C P 

LGAAMVGAVLTALLAGLVSLLCRHKRKQLP CTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT

G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT

M T P B K V P V S B V M G T T L A B M S T P B A T G M T P A ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCGCT

Q T S A G H F P R A C V S S K N L M E K E C C P P W S G D R 

A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGGCCGTGCCATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC

FREGTINVHDVETQFNQYKTEAASRYNLTI TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT

Tyros #3

N L M B K B C C P P W S G D R S P C G Q L S G R G S C Q N I

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AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT

Tyros #32

IKSYLBQASRIWSWLLGAAMVGAVLTALLA
ATCAAAAGCTATCTGGAACAGGCTAGCAGAAATCTGGAGCTGCTGGTGCTGCCATGGTGGGAGCCGTCCTGACAGCCCTCCTGGCT

/UC1R #5

MUCLR #15

S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGGGGAGCCGGAGTGCCTGGGCATTGCCCTCCTGGTCCTGGTCTGGTCTGGTCCTGGTCCTCGCCCTTGCCCTTTGTGTATCTGATTGCCCTC

MC1R #10

FLGAIAVDRYISIFYALRYHSIVTLPRAPRTTCCTCGGCGCTATCGCTATGGCATAGCATTGTGACACTGCCTAGGGCTCCCAGA

cm100 #40

LIMPGQEAGLGQVPLIVGILLVLMAVVLAS

TRP2 #33

T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M B T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA

TDD\_1 #5

L I S P N S V F S Q W R V V C D S L B D Y D T L G T L C N S CTGATTAGCCCTAACTCCGGGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCATACCCTCGGCACACTGTGTAACTCC

MCIP #3

L N S T P T A I P Q L G L A A N Q T G A R C L B V S I S D G CTGAATAGCACCCCACAGCCATTCCCCAACTGGGACTGCCCAACTGGCATCAGACAGGCGCTTAGGTGTCTTGGAAGTGTCCATCTCCGACGGA

Durne #28

HRPLQEVYPEANAPIGHNRESYMVPFIPLY

gp100 #24

TRP2 #11

K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGGTCCACCCTGACTATGGATTACCACACGCATTGGCTCCGGCTCCTGGGACCCAATGGCACACGCCTCAGTTTGCCAAT

gp100 #38

L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T Q CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATTAGCCTCGCCGTCGTGTCCACCCAA

ap100 #30

PEPEGPDASSIMSTESITGSLGPLLDGTATCCCCGAACCCCGAAGCCCCTGACGCTCCATCATGAGCACAGCTCCATCACAGGCTCCCTGGGACCCCTCCTGGATGCCACACACCACA

gp100 #31

S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y
AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACCGTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT

gp100 #5

D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L GACTGTTGGAGAGGCGGACAGGTCAGCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC

Synthetic Protein:

WHRQLYPEWTBAQRLDCWRGGQVSLKVSNDPYILRNQDDRELWPRKFPHRTCKCTGNFAGRNGDFFISSKDLGYDYSYLQDSDPDSPQDYAAPAFLTW
HRYHLLRLBKDMQBMLQBPSFSGHNRESYMVPFIPLYRNGDFFISSKDLGYDLLCLERDLQRLIGNESFALPYWNFATGRNETTEVVGTTPGQAPTAB
PSGTTSVQVPTTEVSTDYYQBLQRDISEMFLQIYKQGGFLGLSNACMBISSPGCQPPAQRLCQPVLPSPACQLVDQLGYSYAIDLPVSVEETPGWPTT
LLVVMGTEDGPIRRNFAGNVARPMVQRLPEPQDVAQCMTVDSLVMKECCFRLGABSANVCGSQQGRNQYKTFAAASRYMLTISDVSVSDVPPPPSAQAA
MSPLWWGFLLSCLGCKILPGAQGQPPRVADLSYTWDFGDSGTLISRALVVTHTYLEPLAEMSTPEATGMTPAEVSIVVLSGTTAAQVIKPRPGSVVV
QLTLAFREGTINVHDVETQFGSAATWGQDVTSVPVTRPALGSTTPPAHDVLHKRQRPVHQGFGLKGAVTLTILLGIFFLCLALIICNAIIDPLIYAFT
SQELRRTLKEVLKFFHRTCKCTGMFAGYNCGDCKFGWTGPNCLSLQKFDMPPFFQNSTPSFRNALEGFDKADSKSTPPSIPSHHSDTPTTLASHSTKT
DASSAANRPALGSTAPPVHNVTSASGSASGSASTCNGTYEGLLRRNQMGRNSMKLPTLKDIRDCTHHSSVPPLTSSMHSTSPQLSTGVSFFFLSFIAY

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YDHVAVLLCLVVFFLAMLVLMAVLYVKLTGDENFT1PYWDWRDAEKCD1CTDEYMGLRLVKRQVPLDCVLYRYGSFSVTLDIVQG1FLQ1YKQGGFIG LSNIKPRPGSVVVQLTLAVIDVITCSSMLSSLCFLGAIAVDRYISIFYRNPGNHDKSRTPRLPSSADVEFCLSLTQYEFDEWLRRYNADISTFPLENA PIGHNRQYNMVSLADTNSLAVVSTQLIMPGQEAGLGQVPLGPVTAQVVLQAAIPLTSCGSSPVPGTTDGHKFGFWGPNCTERRLLVRRNIFDLSAPEK DKLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTAVAAIWVASVVFSTLFIAYYDHVAVLLCLVGTLDSQVMSLHNLVHSFLNGTNALPHSAANGCWYCR RRNGYRALMDKSLHVGTQCALTRRPWHRLFLLRWEQBIQKLTGDENFTIPYWDWAAMAVQGSQRRLLGSLNSTPTAIPQLGLAAVVATIAKNRNLHSP MYCPICCLALSDLLVSQSSMHNALHIYMNGTMSQVQGSANDPIPLLGQHPTNPNLLSPASPFSSWQIVCSRLEEYNYCPICCLALSDLLVSGTNVLBT AVILLLEADPTLISRNSRPSSWETVCDSLDDYNHLVTLTRPALGSTTPPAHDVTSAPDNKAARDAEKCDICTDEYMGGQHPTNPNLLSPASFTFALQL hdpsgylaradlsytwdfgdssgtssadvefclsltqyesgsmdkaanpsprntgptliganaspsialnppgsqkvlpdgqviwgppplhltlivlc PEHPTCGCIFKNFNLFCQCSGNFMGFNCGNCKFGFWGPNCTERRLLQYRRLRKGYTPLMETHLSSKRYTEEAAAPLENAPIGHNRQYNMVPFWPPVTN TEMFVTNPPGSQKVLPDGQVIWVNNTIINGSQVWGGRPTAEAPNTTAGQVPTTEVVGTTPGQAPTASTPGGEKETSATQRSSVPSSTEKNAVSMTSLI YRRRLMKQDFSVPQLPHSSSHWLRLPRILGLLGPNGTQPQFANCSVYDFFVWLHYYSVCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPAAMDLVLKRC llhlavigallavgatkvprnqtgarclevsisdglplslglvslvenalsgsmdkaanfsfrntlegfaspltgiadasspcgqlsgrgscqnills NAPLGPQFPFTGMHYYVSMDALLGGSBIWRDIDFAHEAPAFLEEKQPLLMEKEDYHSLYQSHLAAGQCTBVRADTRPWSGPYILRNQDDRELWPRSVP SSTEKNAVSMTSSVLSSHSPGSGSSTTTPMFNDINIYDLFVWMHYYVSMDALLGGSEQPVYPQETDDACIFPDGGPCPSGSWSQKRSDSLEDYDTLGT  ${\tt LCNSTEDGPIRRNPAGNVAWVNNTIINGSQVWGGQPVYPQETDDACIFPQEKNCEPVVPNAPPAYEKLSAEQSPPPYSPSRSYVPLAHSSSAFTITDQ$ vppsvsvsqlrlekdmqemlqepspslpymnpatgknvcdivpfwppvtnytempvtapdnlgytybaacsvydpfvwlhyysvrdtligpgrpyraid vrrnifdlsapekdkppayltlakhtissdkkghghsyttabkaagigiltvilgvlllifvyvwkthgqynqvlggpvsglsigtgramggpvsgls IGTGRAMLGTHTMEVTVYHRRGISTAPVQMPTAESTGMTPEKVPVSEVMGTTFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRDPIFVVLHSFTDAIFD Bwmkrfnppadawphmlaracqhaqgiarlhkrqrpvhqgfglklltvltvvtgsghasstpggekbtsatqrsfcscpigenspllsgqqvaatfsf  ${\tt RNALEGFDKADGTLDSQVMSLHNLVHSHQSLCNGTPEGPLRRNPCNHDKSRTPRLPPFFPPVTNEELPLTSDQLGYSYAIDLPVSVERKKPPVIRQNI$ hslspqereqplgaldlaqelapighnrwynmvpppppvtneelpltsevsivvlsgttaaqvtttewvettarelpitspqlstgvsppplsphisn lopnssledpyhthgryvppsstdrspyekvsagnggssllflslglvslvenalvvatiaknrnlhspmsflngtnalphsaandpipvvlhsftda IFAVCQCRRKNYGQLDIFPARDTYHPMSEYPTVFFLAMLVLMAVLYVHMLARACQHAQGLARSTNSFRNTVEGYSDPTGKYDPAVRSLHNLALPYNNF ATGKNVCDICTDDLMGSRSNFDSTITDQVPFSVSVSQLRALDGGNKHFLRNQPLFHISNLQFNSSLEDPSTDYYQELQRDISEMSPYEKVSAGNGGSS LSYTNPAVAAASANLAYVIPIGTYGQMKNGSTPMFNDINIYDLFVWRLCQPVLPSPACQLVLHQILKGGSGTYCLNRYGSFSVTLDIVQGIBSABILQ avpsgegdhhafvdsifeqwlqrhrplqevypeanapictddlmgsrsnpdstlispnsvfsqwrvvcfpardtyhpmseyptyhthgryvppsstdr  ${\tt SYTNPAVAAASANLAABHPTCGCIPKNFNLFLALIICNAIIDPLIYMSQVQGSANDPIFLLHHAFVDSIFEQWLQRRNSMKLPTLKDIRDCLSLQKFD$ NPPPPQNSLISRALVVTHTYLEPGPVTAQVVLQAAIPLSFALPYWNFATGRNECDVCTDQLFGAARPDVIGALLAVGATKVPRNQDWLGVSRQLRTKA ALDGGNKHPLRNOPLTPALQLHDPSGYLAECDVCTDQLPGAARPDDPTLISRNSRFSSWEAAMPREDAHFIYGYPKKGHGHSYTTAERAATGKYDPAV RSLHNLAHLFINGTGGQTHLSSSDVSVSDVPPPPSAQSGAGVPGWGIALLVLSPQEREQFLGALDLAKKRVHPDYVITTQHWFFAYLTLAKHTISSDY vipigtygqmkngsgtnvlbtavillleagalvaraavlqqldnvcvlvalaivylialavcqcrknygqldicpqegpdhrdskvslqbkncbpvv PNAPPASVLSSHSPGSGSSTTQGQDVTLAPATEPASDEWMKRFNPPADAWPQELAPIGHNRMYNMVAFHSQELRRTLKEVLTCSWAAPSHQGPAFVTW HRYHLLCLERDLQRLIGNERPMVQRLPEPQDVAQCLEVGLFDTPPPYSNQDPIFVLLHTFTDAVFDEWLRRYNADISTFLGAESANVCGSQQGRGQCTevradtrpwsgyncgdckpgwtgpncerkkppvirqnihslhlflngtggqthlssqdpifvllhtftdavglvsllcrhkrkqlpeekqpllmeked YHSGCKILPGAQGQPPRVCMTVDSLVNKECCPRQLPHSSSHWLRLPRIFCSCPIGENSPLLSGDGGPCPSGSWSQKRSFVYVWKTWGQYWQVLNQDWL GVSRQLRTKAWNRQLYPEWTEAQRLIWRDIDPAHEAPAPLPWHRLFLLRWEQBIQAAMTPGTQSPFFLLLLLTVITVVTGSGHASDKSLHVGTQCALT RRCPQEGFDHRDSKVSLNVTSASGSASGSASTLVHNGTSARATTTPALEGFASPLTGIADASQSSMHNALHIYMNGTRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHAAMLLAVLYCLLWSFQTSAGHFPRACVSSKAFBLTVSCQGGLPKEACMBISSPGCQPPAQVDDRESWPSVFYNRTCQCSGNFMGFNGGN CESABILQAVPSGBGDAFBLTVSCQGGLPKETVCDSLDDYNHLVTLCNGTYEGLLRRNQMGLLSNAPLGPQFPFTGVDDRBSWPSVFYNRTYEKLSAE QSPPPYSPAAIVGILLVLMAVVLASLIYRRRLMKQDFSVPGIGILTVILGVLLLIGCWYCRRRNGYRALMYSYLQDSDPDSPQDYIKSYLEQASRIWS wlqqqdvtlapatepasgsaatwqqdvtsvpvtscgsspvpgttdghrptaeapnttagqvplvhngtsaratttpaskstpfsipshhsdteetpgw PTTLLVVMGTLVALVGLFVLLAFLTTTEWVETTARELPIPEPEGPDASSIMSTEGAVTLTILLGIFFLCWGPFFLHLTLIVLCPLGAAMVGAVLTALL aglvsllcrhkrkqlpgalvaraavlqqldnvidvitcssmlsslchtpbkvpvsbvmgttlaemstpbatgmtpaqtsaghppracvssknlmbkec CPPWSGDRALRYHSIVTLPRAPRAVAAIWVASVVFSTLFREGTINVHDVETQFNQYKTEAASRYNLTINLMEKECCPPWSGDRSPCGQLSGRGSCQNI IKSYLEQASRIWSWLIGAAMVGAVLTALLAPTTLASHSTKTDASSTHHSSVPPLTSSWHSSGAGVPGWGIALLVLVCVLVALAIVYLIALPIGAIAVD RYISIFYALRYHSIVTLPRAPRLIMPGQBAGLGQVPLIVGILLVLMAVVLASTLVALVGLFVLLAFLQYRRLRKGYTPLMBTLISPNSVFSOMRVVCD Sledydtlgtlcnsinstptaipqlglaanqtgarclevsisdghrplqevypeanapighnresymvppiplyepsgttsvqvpttevistapvqnp TABSTGKKRVHPDYVITTQHNLGLLGPNGTQPQPANLHQILKGGSGTYCLNVSLADTNSLAVVSTQPBPBGPDASSIMSTBSITGSLGPLLDGTATSI TGSLGPLLDGTATLRLVKRQVPLDCVLYDCWRGGQVSLKVSNDGPTLIGANASFSIAL

### Synthetic DNA:

TTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTATGCCGCTCCCGCTTTCCTCACCTGG CACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTTCTCTCCGGCCATAACAGAGAGTCCTACATGGTGCCTTT ATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAAACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAA CCCTCCGGCACACCTCCGTGCAAGTGCCTACCACAGAGGTCAGCACAGACTATTACCAAGAGGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAAT  $\tt CTATAAGCAAGGCGGATTCCTCGGCCTCAGCAATGCCTGTATGGAAATCTCCAGCCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGC$ TCCCCTCCCCGCTTGCCAACTGGTCGACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACA CTGCTCGTGGTCATGGGAACCGAAGACGGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGGCCCATGGTGCAAAGGCTCCCCGAACCCCAAGA GAAACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCCTTTCTCCGCCCAAGCCGCT AAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTCATCAAATTCAGACCCGGAAGCGTCGTGGTC CAGCTCACCTCGCCTTTAGGGAAGGCACAATCAATGTGCATGACGTCGAGACACAGTTTGGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGT GCCTGTGACAAGGCCTGCCCTCGCCTCCACCACCACCACCCCCTGCCCATGACGTCCTGCATAAGAGACAGAGACCCGTCCACCAAGGCTTTGGCCTCAAGG AGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTCAAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTG 

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GACGCTAGCTCCGCCGCTAACAGACCCCGCTCTGGGAAGCACAGCCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAG  ${\tt TACGATCACGTCGCCTCTGCCTCGTGGTCTTCTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTCAAGCTCACCGGAGACGAAAA}$ TCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATTTTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGA CTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCTGTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTGTG CTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTCTATAGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCG CTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAATTCGATGAGTGGCTGAGAAGGTATAACGCTGACATTAGCACATTCCCTCTGGAAAACGCT CCCATTGGCCATAACAGACAGTATAACATGGTGTCCCTGGCTGACACAACTCCCTGGCTGTGGTCAGCACACACCTCATCATGCCCGGACAGGAAGC CGGACTGGGACAGGTCCCCCTCGGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCA CGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTCGGCACACTGG AGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGACCCTGGCACAGACTGTTTCTGCTCAG GTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGGGCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGC TCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCTGTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCT ATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCCCAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAG CCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTCGGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGC AAATCGTCTGCTCCAGGCTCGAGGAATACAATTACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACA GCCGTCATCCTCCTGCTCGAGGCTGACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAA CCATCTGGTCACCCTCACCAGACCCGGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAAGCCGCTAGGGATGCCG AAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTTACCTTTGCCCTCCAGCTC CACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACAAGCTCCGCCGATGTGGAATTCTGTCT GTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACAGGCCCTACCCTCATCGGAGCCAATGCCTCCTTCT CCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATTTGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGT CCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTTTGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATT CGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTCCAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCATCTGTCCAGCA GTGGGGCGGAAGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACACCCCTGGCCAAGCCCCTACCG TACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATTCTGGGACTGCTCGG ATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTGCCGCTATGGATCTGGTCCTGAAAAGGTGT CTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGAAACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAG CGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTCAGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCC TCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCCAGCCCTTGCGGACAGCTCAGCGGGAAGGCTGTCAGAATATCCTCCTGTCC AACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGAATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGA CTTTGCCCATGAGGCTCCCGCTTTCCTCGAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCCG GCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGAAGCGTCCCC TATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGGAACAGCCTGTGTATCCCCCAAGAGACAG ACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCCGACTCCCTGGAAGACTATGACACACTGGGAACC CTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCTTGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGG AGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCTCAGGAAAAGAATTGCGAACCCGTCGTGCCTAACGCTCCCCCTGCCTATG AGAAACTGTCCGCCGAACAGTCCCCCCCCCCCCTATAGCCCTAGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAG GTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGACTGGAAAAGGATATGCAAGAGATGCTGCAAGAGCCTAGCTTTAGCCTCCCCTATTGGAATTTCGC TACCGGAAAGAATGTGTGTGACATTGTGCCTTTCTGGCCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATG  ${\tt AGGCTGCCTGGTGTGTGTGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCGGGCAGACCCTATAGGGCTATCGAT}$ GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGATAAGAAAGG AAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGGCAGAGCCATGGGCGACCCGTCAGCGGACTGTCC ATCGGAACCGGAAGGGCTATGCTCGGCACACACACAATGGAAGTGACAGTGTATCACAGAAGGGGAATCTCCACCGCTCCCGTCCAGATGCCCACAGC ATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGAGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGAT GAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCTCACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAG GCAAAGGCCTGTGCATCAGGGATTCGGACTGAAACTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGA  ${\tt AAGAGACAAGCGCTACCCAAAAGGTCCTTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCTACCTTTAGCTTT$ AGGANTECCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCATAGCCATCAGTCCCTGTGTAA AACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTCGAGAGAAAACCACCCCTGTGATTAGGCAAAACATT CACTCCCTGTCCCCCAAGAGAGAGAGAGCAATTCCTCGGCGCTCTGGATCTGGCTCAGGAACTGGCTCCCATTGGCCATAACAGAATGTATAACATGGT  ${\tt CAGAGTGGGTAAACCACAGCCAGAGAGCTCCCCATTACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAAT}$  $\tt CTGCAATTCAATAGCTCCCTGGAAGACCCTTACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGC$ TCCACTCCCCATGAGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCT ATCTTTGCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACAGT GTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGAAGCACAAACT

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 ${\tt CCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCTCTGCCTTACTGGAACTTT}$ GCCACAGGCAAAAACGTCTGCGGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACAATCACAGACCAAGTGCCTTTCTCCGT GTCCGTGTCCCAGCTCAGGGCTCTGGATGGCGGAAACAACACTTTCTGAGAAACCACCCCTCTTCCATATCTCCAACCTCCAGGTTTAACTCCAGCC CTGTCCTACACAAACCCTGCCGCCGCCGCCCCCCCCCAATCTGGCTTACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACACC TCAAGGGAGGCTCCGGCACATACTGTCTGAATAGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAA GGCTAACGCTCCCATTTGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGG CCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTATATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCG TCGACTCCATCTTTGAGCAATGGCTCCAGAGAAGGAATAGCATGAAGCTCCCCACACTGAAAGACATTAGGGATTGCCTCAGCCTCCAGAAATTCGAT AACCCTCCCTTTTTCCAAAACTCCCTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCA GACCCGATGTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAATGCGATGT GTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAAGCCGCTATGCCTAGGG AAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGGACACTCCTACACAACCGCTGAGGAAGCCGCTACCGGAAAGTATGACCCTGCCGTC CTTTAGCGCTCAGTCCGGCGCTGGCGTCCCCGGATGGGGAATCGCTCTGCTCGTGCTCAGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACC TCGCCAAAAAGAGAGTGCATCCCGATTACGTCACACACCCAACACTGGTTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTAT GTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCCGGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGT GAAAGAATTACGGACAGCTCGACATTTGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTC  ${\tt CCCAATGCCCCTCCCGCTAGCGTCCTGTCCAGCCATAGCCCTGGCTCCGGCTCCAGCACAAGCCCAAGGCCCAAGACGTCACCCTCGCCCCTGCCACAGA}$ GCCTGCCTCCGACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGG TCGCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCCTTCTCCCACCAAGGCCCTGCCTTTGTGACATGG  ${\tt CATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGCATATGGTCCAGAGACTGCCTGAGCCTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGGATGTCAGATGATGTCAGATGATGTCAGATGTCAGATGTCAGATGTCAGATGTCAGATGTCAGATGTCAGATGTCAGATGTCAGATGATGTCAGATGATGTCAGATGTCAG$ TCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAATCAGGATCCCATTTTGGTCCTGCTCCACACATTCACAGACGCTGTGTTTG ACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTTCTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGGAAGGGGACAGTGTACC GAAGTGAGGCCGATACCAGACCCTGGAGCGGATACAATTGCGGAGACTGTAAGTTTGGCTGGACCGGACCCAATTGCGAAAGGAAAAAGCCTCCCGT CCTTTACCGATGCCGTCGGCCTCGTGTCCCTGCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAAACAGCCTCTGCTCATGGAAAAGGAAGAC TATCACTCCGGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAG gcccttgccctagcggaagctggagccaaaagagaagctttgtgtatgtgtggaagacatggggacagtattggcaagtgctcaaccaagactggctg TCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAAGCCGCTATGACACCCGGAACCCAAAGCCCTT TCTTTCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCCGACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACC AGAAGGTGTCCCCAAGAGGGATTCGATCACAGAGACTCCAAGGTCAGCCTCAACGTCACCTCCGCCTCCGGCTCCGGCTCCGGCTCCGCCTCCACCCT CGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCCGCTCTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCA TGCATAACGCTCTGCATATCTATATGAATGGCACAAGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCC GCTTTCGTCACCTGGCACAGATACCATGCCGCTATGCTCCTGGCTGTCTTACTGTCTGCTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAG AGCCTGTGTGTCCAGCAAAGCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAAC CCCCTGCCCAAGTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAAC TGTGAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAAACCGT CTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGACTGCTCAGCAATG CCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACATACGAAAAGCTCAGCGCTGAG GAAACAGGATTTCTCCGTGCCTGGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTCCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCT ATAGGGCTCTGATGTACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCC TGGCTCCAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTCAC CTCCTGCGGAAGCTCCCCCGTCCCCGGAACCACAGACGGACACAGACCCACAGCCGAAGCCCCTAACACACCGCTGGCCAAGTGCCTCTGGTCCACA CCCACAACCCTCCTGGTCGTGGTCGCCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTCACCACCAACCGAATGGGTCGAGACAAC CGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAAGGCGCTGTGACACTGACAATCCTCCTGGGAATCT TTTTCCTCTGCTGGGGCCCTTTCTTCTGCATCTGACACTGATTGTCCTCTGCCCCTCTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTC GCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCTGGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCAT CGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGTATGACACCCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGT CCACCCCTGAGGCTACCGGAATGACACCCGCTCAGACAAGCGCTGGCCATTTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGGAGAAAGAGTGT TGCCCTCCCTGGAGCGGAGACAGAGCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGT TCACCATTAACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT CTGGCTGGGGCATTGCCCTCCTGGTCCTGGTCTGGTCCTGGTCGCCCATTGTGTATCTGATTGCCCTCTTCCTCGGCGCTATCGCTGTGGAT  ${\tt AGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGACTGATTATGCCTGGCCAAGAGGCTGGCCTCGG$ TTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACACTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGAT AGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCCCTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTACCCAATCAGACAGG CGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGACACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCT

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Melanoma cancer Specific Savine Scramble process

ATATGGTCCCTTTATCCCTCTGTATGAGCCTAGCGGAACCACAAGCGTCCAGGTCCCACAACCGAAGTGATTAGCACAGCCCTGTGCAAATGCCT
ACCGCTGAGTCCACCGGAAAGAAAAGGGTCCACCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCA
GTTTGCCAATCTGCATCAGATTCTGAAAGGCGGAACCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTTCCACCC
AACCCGAAGCCCGAAGGCCCTAGCTCCATCATGAGCACAGAGCCCACAGCCTCCTCGGACCCCTCCTGGATGGCACAGCCACAGCATT
ACCGGAAGCCTGGCCCTCTGCTCGACGGAACCGCTACCCTCCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCCTCTGTATGACTGTTGGAGAGG
CGGACAGGTCAGCCTCAAGGTCACCAATGACGGACCCACACTGATTGGCGCTAACGCTTAGCATTTGCCCTC

```
Scramble - Output File
Scramble version: 0.1 beta, 08/02/1999
Num. genes : 10
Num. segments : 121
Segment length : 30
Segment over
Segment overlap : 15
Segments in original order:
Gene
       : BAGE
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S
: BAGE
Segment# : 2
Offset
       : 16
1st Codon : 1
 LLQARLMKEESPVVSWRLEPBDGTALCFIF
CTGCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTT
       : BAGE
Gene
Segment# : 3
Offset
       : 31
1st Codon : 1
 WRLEPEDGTALCFIFAA
TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC
Gene
       : GAGE-1
Segment# : 1
Offset
       : 1
1st Codon : 1
A A M S W R G R S T Y R P R P R R Y V B P P E M I G P M R P
GCCGCTATGTCCTGGAGAGGCCAGAAGCACATACAGACCCAGAAGCTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT
Segment# : 2
Offset
       : 16
1st Codon : 1
RRYVEPPEMIGPMRPEQFSDEVEPATPEEG
AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA
       : GAGE-1
Gene
Segment# : 3
       : 31
Offset
1st Codon : 1
EQFSDBVEPATPEEGEPATQRQDPAAAQEG
GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAGGCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGA
Gene
       : GAGE-1
Segment# : 4
Offset
       : 46
1st Codon : 1
EPATQRQDPAAAQEGEDEGASAGQGPKPEA
GAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTAGGCCTAAGCCTGAGGCT
       : GAGE-1
Segment# : 5
Offset
       : 61
1st Codon : 1
```

Figure 27 (Cont)

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```
E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E
 GAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATGCCAAGAGCAAGGCCATCCCCAAACCGGATGCGAATGCGAA
 Gene
         : GAGE-1
 Segment# : 6
         : 76
 Offset
 1st Codon : 1
  D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E
 GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA
 Gene
         : GAGE-1
 Segment# : 7
 Offset
         : 91
 1st Codon : 1
 D G P D G Q B M D P P N P B B V K T P B B B M R S H Y V A Q
 GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGGTCAAGACACCCCGAAGAGGGAAATGAGAAGCCATTACGTCGCCCAA
 Gene
         : GAGE-1
 Segment# : 8
 Offset
        : 106
 lst Codon : 1
 V K T P E E E M R S H Y V A Q T G I L W L L M N N C F L N L
 GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC
         : GAGE-1
 Gene
 Segment# : 9
 Offset
        : 121
 1st Codon : 1
 T G I L W L L M N N C P L N L S P R K P A A
ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT
Gene
         : gp100In4
Segment# : 1
Offset
        : 1
1st Codon : 1
 A A S W S Q K R S F V Y V W K T W G B G L P S Q P I I H T C
GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT
Gene
        : qp100In4
Segment# : 2
Offset
        : 16
1st Codon : 1
 T W G E G L P S Q P I I H T C V Y F F L P D H L S F G R P F
ACCTGGGGCGAAGGCCTCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT
        : gpl00In4
Gene
Segment# : 3
Offset
        : 31
1st Codon : 1
 V Y F F L P D H L S F G R P F H L N F C D F L A A
GTGTATTTCTTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC
        : MAGE-1
Gene
Segment# : 1
Offset
1st Codon : 1
A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V
GCCGCTATGTCCCTGGAACAGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC
Gene
        : MAGE-1
Segment# : 2
Offset
        : 16
1st Codon : 1
B A L B A Q Q B A L G L V C V Q A A T S S S P L V L G T L
Gene
        : MAGE-1
Segment# : 3
Offset
       : 31
1st Codon : 1
Q A A T S S S P L V L G T L B B V P T A G S T D P P Q S P
CAGGCTGCCACAAGCTCCAGCTCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCCAAAGCCCT
```

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: MAGE-1 Segment# : 4 Offset : 46 1st Codon : 1 B B V P T A G S T D P P Q S P Q G A S A F P T T I N F T R Q : MAGE-1 Segment# : 5 Offset : 61 1st Codon : 1 Q G A S A F P T T I N F T R Q R Q P S E G S S S R E E E G P : MAGE-1 Gene Segment# : 6 Offset : 76 1st Codon : 1 RQPSEGSSSREEEGPSTSCILESLFRAVIT : MAGE-1 Gene Segment# : 7 Offset : 91 1st Codon : 1 S T S C I L E S L F R A V I T K K V A D L V G F L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA : MAGE-1 Segment# : 8 Offset 1st Codon : 1 K K V A D L V G F L L K Y R A R B P V T K A B M L B S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT Gene : MAGE-1 Segment# : 9 Offset 1st Codon : 1 AREPVTKAEMLESVIKNYKHCFPEIFGKAS GCCAGAGAGCCTGTGACAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC : MAGE-1 Gene Segment# : 10 : 136 Offset 1st Codon : 1 K N Y K H C F P E I F G K A S E S L Q L V F G I D V K E A D AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT : MAGE-1 Gene Segment# : 11 Offset : 151 ESLQLVFGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCC Gene : MAGE-1 Segment# : 12 Offset : 166 1st Codon : 1 PTGHSYVLVTCLGLSYDGLLGDNQIMPKTG CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA Gene : MAGE-1 Segment# : 13 Offset : 181 1st Codon : 1 Y D G L L G D N Q I M P K T G F L I I V L V M I A M E G G H 

Gene : MAGE-1

### 186/216

Segment# : 14 Offset : 196 1st Codon : 1 F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V TTCCTCATCATCGTCGTCGTCGTCGTCGTATGGAAGGCGGACACGCTCCCGAAGAGGGAAATCTCGGGAGGAACTGTCCGTGATGGAGGTC : MAGE-1 Segment# : 15 Offset : 211 1st Codon : 1 APEEELSVMEVYDGREHSAYGEPRKL GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGGGTCATGGAAGTGTATGACGGAAGGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC : MAGE-1 Gene Segment# : 16 Offset : 226 1st Codon : 1 Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGGCAGAGAGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAAAATACCTCGAGTATAGGCAA : MAGE-1 Gene Segment# : 17 Offset : 241 1st Codon : 1 L T Q D L V Q E K Y L B Y R Q V P D S D P A R Y E F L W G P : MAGE-1 Segment# : 18 Offset : 256 1st Codon : 1 V P D S D P A R Y E F L W G P R A L A R T S Y V K V L R Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC Gene : MAGE-1 Segment# : 19 1st Codon : 1 RALAETSYVKVLKYVIKVSARVRFFFPSLR : MAGE-1 Gene Segment# : 20 Offset : 286 1st Codon : 1 I X V S A R V R F F F P S L R E A A L R E E E G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGAAGAGGAAGGCGTCGCCGCT Gene : MAGE-3 Segment# : 1 Offset : 1 1st Codon : 1 A A M P L B Q R S Q H C K P E B G L B A R G B A L G L · V G A GCCGCTATGCCTCTGGAACAGAGAGACACACTGTAAGCCTGAGGAAGGCCTCGAGGGCTAGGGGGAGAGGCTCTGGGACTGGTCGGCGCT Segment# : 2 Offset : 16 1st Codon: 1 B G L B A R G E A L G L V G A Q A P A T B E Q B A A S S S S GAGGGACTGGAAGCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC : MAGE-3 Gene Segment# : 3 Offset : 31 1st Codon : 1 Q A P A T B B Q B A A S S S S T L V B V T L G B V P A A B S Gene : MAGE-3 Segment# : 4 Offset : 46

## 187/216

1st Codon : 1 T L V B V T L G E V P A A B S P D P P Q S P Q G A S S L P T ACCUTEGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTCCCCAAAGCCCTCAGGGAGCCTCCAGCCTCCCACA : MAGE-3 Gene Segment# : 5 Offset 1st Codon : 1 P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S CCCGATCCCCTCAGTCCCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC Gene : MAGE-3 Segment# : 6 1st Codon : 1 T M N Y P L N S Q S Y E D S S N Q E E E G P S T P P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAGGAAGAGGAAGGGCCCTAGCACATTCCCTGACCTCGAGTCC Gene : MAGE-3 Segment# : 7 Offset : 91 1st Codon : 1 NQBEEGPSTFPDLESEPQAALSRKVABLVH AACCAAGAGGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT Gene : MAGE-3 Segment# : 8 Offset : 106 1st Codon : 1 E F Q A A L S R K V A E L V H F L L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTTGACAAAGGCT : MAGE-3 Gene Segment# : 9 : 121 Offset 1st Codon : 1 F L L K Y R A R E P V T K A E M L G S V V G N N Q Y F P P TTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTGGTCGGCAATTGCCAATACTTTTCCCT Segment# : 10 Offset : 136 1st Codon : 1 B M L G S V V G N W Q Y F F P V I F S K A S S S L Q L V F G Gene : MAGE-3 Segment# : 11 Offset : 151 1st Codon : 1 V I F S K A S S S L Q L V F G I E L M E V D P I G H L Y I F GTGATTTTCTCCAAGGCTAGCTCCAGCCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT Gene : MAGE-3 Segment# : 12 Offset : 166 1st Codon : 1 I E L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT Gene : MAGE-3 Segment# : 13 Offset 1st Codon : 1 A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT : MAGE-3 Gene Segment# : 14 Offset : 196 1st Codon : 1 Q I M P K A G L L I I V L A I I A R E G D C A P E R K I W E

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Gene
        : MAGE-3
 Segment# : 15
 Offset
       : 211
 1st Codon : 1
 I A R B G D C A P B B K I W B B L S V L E V F E G R E D S I
 ATCGCTAGGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATT
Gene
        : MAGE-3
Segment# : 16
Offset
       : 226
1st Codon : 1
 ELSVLEVFEGREDSILGDPKKLLTOHFVOE
GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA
       : MAGE-3
Gene
Segment# : 17
Offset
       : 241
1st Codon : 1
 LGDPKKLLTQHPVQENYLEYRQVPGSDPAC
Gene
       : MAGE-3
Segment# : 18
Offset
       : 256
1st Codon : 1
 N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y
AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT
       : MAGE-3
Segment# : 19
Offset
       : 271
1st Codon : 1
 Y R F L W G P R A L V E T S Y V K V L H H M V K I S G G P H
TACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT
Gene
       : MAGE-3
Segment# : 20
Offset
1st Codon : 1
 V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E
GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACCATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA
       : MAGE-3
Gene
Segment# : 21
Offset
       : 301
1st Codon : 1
ISYPPLHEWVLREGERAA
Gene
       : PRAME
Segment# : 1
Offset
       : 1
1st Codon : 1
AAMERRRLWGSIQSRYISMSVWTSPRRLVR
GCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA
Gene
      : PRAME
Segment# : 2
Offset
      : 16
1st Codon : 1
Y I S M S V W T S P R R L V B L A G Q S L L K D B A L A I A
TACATTAGCATGAGGGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT
Gene
       : PRAME
Segment# : 3
Offset
      : 31
1st Codon : 1
LAGQSLLKDBALAIAALELLPRELFPLFM
CTGGCTGGCCAAAGCCTCCTGAAAGACGAAGCCCTCGCCATTGCCGCTCTTGGAACTGCTCCCCAGAGAGGCTCTTCCCCCCTCTTCATG
```

PCT/AU01/00622 WO 01/090197

### 189/216

Gene : PRAME Segment# : 4 Offset : 46 1st Codon : 1 A L B L L P R B L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC Gene : PRAME Segment# : 5 Offset : 61 1st Codon : 1 A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTTGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA : PRAME Segment# : 6 Offset 1st Codon : 1 Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGCCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA Gene : PRAME Segment# : 7 Offset : 91 1st Codon : 1 G Q H L H L E T F K A V L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCAGCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCAAGAGGTCAGGCCTAGGAGATGGAAA : PRAME Segment# : 8 Offset : 106 1st Codon : 1 LDVLLAQBVRPRRWKLQVLDLRKNSHQDPW CTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGTGGAAGCTCCAGGTCCTGGATCTGGAAAGAATAGCCATCAGGATTTCTGG : PRAME Gene Segment# : 9 1st Codon : 1 LQVLDLRKNSHQDFWTVWSGNRASLYSFPE CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA : PRAME Gene Segment# : 10 : 136 Offset 1st Codon : 1 T V W S G N R A S L Y S P P B P E A A Q P M T K K R K V D G ACCGTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAAGGTCCACGGA Gene : PRAME Segment# : 11 Offset : 151 1st Codon : 1 P B A A Q P M T K K R K V D G L S T B A B Q P F I P V B V L CCCGAAGCCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC Gene ': PRAMB Segment# : 12 Offset : 166 1st Codon : 1 LSTEAEQPFIPVEVLVDLFLKEGACDELFS : PRAME Segment# : 13 Offset : 181 1st Codon : 1 V D L F L K B G A C D B L F S Y L I B K V K R K K N V L R L

: PRAME Gene Segment# : 14

GTGGATCTGTTTCTGAAAGGGGGGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGGAAAAGGAAAAGGAATGTGCTCAGGCTC

### 190/216

Offset : 196 1st Codon : 1 Y L I B K V K R K K N V L R L C C K K L K I P A M P M Q D I TACCTCATCGAAAAGGTCAAGAAAAGAAAACGTCCTGAGACTGTGTTGCAAAAAGGTCAAGATTTTCGCTATGCCTATGCAAGACATT : PRAME Gene Segment# : 15 Offset : 211 1st Codon : 1 C C K K L K I F A M P M Q D I K M I L K M V Q L D S I K D L TGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC : PRAME Gene Segment# : 16 Offset : 226 1st Codon : 1 K M I L K M V Q L D S I E D L E V T C T W K L P T L A K P S AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC : PRAME Gene Segment# : 17 Offset : 241 E V T C T W K L P T L A K P S P Y L G Q M I N L R R L L L S GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC Gene : PRAME Segment# : 18 Offset : 256 1st Codon : 1 PYLGQMINLRRLLLSHIHASSYISPEKEEO CCCTATCTGGGACAGATGATCAGTCAGAGAAGGCTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGGAAAAGGAAGAGCAA Gene : PRAME Segment# : 19 Offset : 271 1st Codon : 1 HIHASSYISPEKEEQYIAQFTSQFLSLQCL CACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC : PRAME Gene Segment# : 20 Offset 1st Codon : 1 Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTGTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC Gene : PRAME Segment# : 21 : 301 Offset 1st Codon : 1 Q A L Y V D S L F F L R G R L D Q L L R H V M N P L B T L S CAGGCTCTGTATGTGGATAGCCTCTTCTTCTGAGAGGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCC : PRAME Gene Segment# : 22 Offset : 316 1st Codon : 1 D Q L L R H V M N P L B T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC Gene : PRAME Segment# : 23 Offset : 331 1st Codon : 1 I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA : PRAME Gene Segment# : 24 : 346 Offset 1st Codon : 1

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```
Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L
 CAGTCCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCGGCGTCATGCTCACCGATGTGTCCCCCGAACCCCTCCAGGCTCTGCTC
 Gene
         : PRAME
 Segment# : 25
 Offset
         : 361
 1st Codon : 1
  V M L T D V S P B P L Q A L L B R A S A T L Q D L V P D B C
 GTGATGCTGACAGACGTCAGCCCTGAGCCCTCTGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGATCTGGTCTTCGATGAGTGT
 Gene
        : PRAME
 Segment# : 26
 Offset
        : 376
 1st Codon : 1
 E R A S A T L Q D L V P D E C G I T D D Q L L A L L P S L S
 GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGGAATCACAGACGATCAGCTCCTGGCTCCCCTGCCCTGTCC
 Gene
         : PRAME
 Segment# : 27
        : 391
 1st Codon : 1
 G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I
 GGCATTACCGATGACCAACTGCTCGCCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT
         : PRAME
 Gene
 Segment# : 28
 Offset
1st Codon : 1
 H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L
CACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGCATCTGATTGGCCTC
        : PRAME
Gene
Segment# : 29
Offset
        : 421
1st Codon : 1
 S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L E S Y
AGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT
Gene
        : PRAME
Segment# : 30
Offset
        : 436
1st Codon : 1
 SNLTHVLYPVPLESYEDIHGTLHLERLAYL
AGCAATCTGACACACGTCCTGTATCCCGTCCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC
Gene
        : PRAME
Segment# : 31
       : 451
1st Codon : 1
 B D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S
GAGGATATCCATGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCC
        : PRAME
Gene
Segment# : 32
Offset
1st Codon : 1
 HARLRBLLCELGRPSMVWLSANPCPHCGDR
CACGCTAGGCTCAGGGAACTGCTCTGCGAACTGGGAAGGCCTAGCATGGTGTGGCTGTCCGCCAATCCCTGTCCCCATTGCGGAGACAGA
        : PRAME
Gene
Segment# : 33
Offset
        : 481
1st Codon : 1
MVWLSANPCPHCGDRTFYDPEPILCPCFMP
ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT
        : PRAME
Gene
Segment# : 34
Offset
       : 496
1st Codon : 1
T F Y D P B P I L C P C F M P N A A
ACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT
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Gene : TRP2IN2 Segment# : 1 Offset 1st Codon : 1 A A L M E T H L S S K R Y T B E A G G F F P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA : TRP2IN2 Gene Segment# : 2 Offset : 16 1st Codon : 1 BAGGFFPWLKVYYYRFVIGLRVWQWEVISC GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT : TRP2IN2 Segment# : 3 Offset : 31 1st Codon : 1 FVIGLRVWQWBVISCKLIKRATTRQPAA TTCGTCATCGGACTGGGAGTGTGGCAGTCGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCCACAACCAGACAGCCTGCCGCT : NYNSOla Gene Segment# : 1 1st Codon : 1 AAMQAEGRGTGGSTGDADGPGGPGIPDGPG GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA Gene : NYNSOla Segment# : 2 Offset : 16 D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGCCCTGGCGGAAACGCTGGCGGACACGCGAGAGGCTGCCGCTACCGGAGGCAGA : NYNSOla Gene Segment# : 3 Offset : 31 1st Codon : 1 G N A G G P G E A G A T G G R G P R G A G A A R A S G P G G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGACCCAGAGGCGCTGGCGAGAGCCTCCGGCCCTGGCGGA Gene : NYNSOla Segment# : 4 Offset : 46 1st Codon : 1 G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGGAGCCGCTAGGGGCCGGACCCGGAGGCGGAGCCCCTAGGGGACCCCCATGGCGGAGCCGCTAGCGGACTGAAT Gene : NYNSOla Segment# : 5 : 61 1st Codon : 1 G A P R G P H G G A A S G L N G C C R C G A R G P E S R L L Gene : NYNSOla Segment# : 6 Offset : 76 1st Codon : 1 G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA : NYNSOla Gene Segment# : 7 Offset : 91 E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTC Gene : NYNSOla

### 193/216

Segment# : 8 Offset : 106 1st Codon : 1 LARRSLAQDAPPLPVPGVLLKEFTVSGNIL CTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGGCGTCCTGCCTCAAGGAATTCACAGTGTCCGGCAATATCCTC : NYNSO1a Gene Segment# : 9 Offset 1st Codon : 1 P G V L L K B F T V S G N I L T I R L T A A D H R Q L Q L S  ${\tt CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGTCC}$ Cene : NYNSOla Segment# : 10 Offset : 136 1st Codon : 1 TIRLTAADHRQLQLSISSCLQQLSLLMWIT ACCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA Gene : NYNSOla Segment# : 11 Offset : 151 1st Codon : 1 I S S C L Q Q L S L L M W I T Q C F L P V F L A Q P P S G Q Gene : NYNSO1a Segment# : 12 Offset : 166 1st Codon : 1 QCFLPVFLAQPPSGQRRAA CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAAGGGCTGCC Gene : NYNSO1b Segment# : 1 Offset : 1 1st Codon : 1 A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT Gene : NYNSO1b Segment# : 2 Offset : 16 Q G A M L A A Q E R R V P R A A E V P G A Q G Q Q G P R G R CAGGGAGCCATGCTGGCTGCCCAAGAGAGAGGGTCCCCAGAGCCGCTGAGGTCCCCGGAGCCCAAGGGCCAACAGGGACCCAGAGGCAGA Gene : NYNSO1b Segment# : 3 Offset : 31 1st Codon : 1 A B V P G A Q G Q Q G P R G R B B A P R G V R M A A R L Q G GCCGAAGTGCCTGGCGCTCAGGGACAGCCAAGGCCCTAGGGGAAGGGGAAGAGGCTCCCAGAGGCGTCAGGATGGCCGCTAGGCTCCAGGGA Gene : NYNSO1b Segment# : 4 Offset : 46 BBAPRGVRMAARLQGAA GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC Gene : LAGE1 Segment# : 1 Offset A A M Q A E G Q G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCCAAGGCACAGGCGGAAGCACAGGCGGATGCCGGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA Gene : LAGE1 Segment# : 2 Offset

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1st Codon : 1
  DADGPGGPGGPGGNAGGPGATGGR
 GACGCTGACGGACCCCGGAGGCCCTTGCCATTCCCGATGCCCTTGCCGGAAACGCTGGCGGACCCGGAGGGCTGGCCTTACCGGAGGCAGA
 Gene
         : LAGE1
 Segment# : 3
 Offset
        : 31
 1st Codon : 1
  G N A G G P G B A G A T G G R G P R G A G A R A S G P R G
 GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGCGCTGGCGCTGCCAGAGCCTCCGGCCCTAGGGGA
         : LAGE1
 Gene
 Segment# : 4
        : 46
 Offset
 1st Codon : 1
 G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D
 GGCCCTAGGGGAGCCGGAGCCGCTAGGGCTAGCGGACCCCAGAGGCGGAGCCCCTAGGGGAGCCCCCATGGCGGAGCCGCTAGCGCTCAGGAT
 Gene
        : LAGE1
 Segment# : 5
 Offset
        : 61
 1st Codon : 1
 G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L
 GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC
Gene
        : LAGE1
Segment# : 6
Offset
       : 76
1st Codon : 1
 G R C P C G A R R P D S R L L Q L H I T M P F S S P M B A B
GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA
Gene
Segment# : 7
Offset
       : 91
1st Codon : 1
 Q L H I T M P F S S P M B A B L V R R I L S R D A A P L P R
CAGCTCCACATTACCATGCCCCTTTAGCTCCCCCATGGAGGCTGAGGAGGATTCTGTCCAGGGATGCCGCTCCCCCAGA
        : LAGE1
Gene
Segment# : 8
Offset
       : 106
1st Codon : 1
 L V R R I L S R D A A P L P R P G A V L K D P T V S G N L L
\tt CTGGTCAGGAGAATCCTCAGGAGAGGCGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC
Gene
        : LAGE1
Segment# : 9
Offset
       : 121
1st Codon : 1
PGAVLKDFT V S G N L L F I R L T A A D H R Q L Q L S
CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC
       : LAGE1
Segment# : 10
Offset
       : 136
1st Codon: 1
FIRLT A A D H R Q L Q L S I S S C L Q Q L S L L M W I T
TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA
Segment# : 11
Offset
       : 151
1st Codon: 1
ISSCLQQLSLLMWITQCFLPVFLAQAPSGQ
Gene
Segment# : 12
Offset
       : 166
1st Codon : 1
QCFLPVFLAQAPSGQRRAA
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CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

Segments in scrambled order:

MAGE-1 #15

A P B B B I W B B L S V M B V Y D G R B H S A Y G B P R K L GCCCCTGAGGAAGAGATTTGGGAAGACTCAGGAAGGTGTATGACGGAAGGGAACACTCCGCCTTATGGCGAACACCCAGAAAGCTC

MAGE-1 #4

PRAME #10

MAGE-3 #14

Q I M P K A G L L I I V L A I I A R E G D C A P E E K I W E CAGATTATGCCTAAGGCTGGCCTCCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA

PRAME #9

PRAME #8

L D V L L A Q E V R P R R W K L Q V L D L R K N S H Q D F W CTGGATGTCCTGGTCCTGGTCAGGAAGTGAGACCCAGAAGGTGGAAGCTCCAGGTCCTGGATCTGAGAAGAATAGCCATCAGGATTTCTGG

NYNSOLD #2

PRAME #24

Q S P S V S Q L S V L S L S G V M L T D V S P B P L Q A L L CAGTCCCCTCCGGCTCAGCGTCCTGTCCCGGCTCATGCTCACCGATGTTCCCCGAACCCCTCCAGGCTCTGTC

MAGE-1 #17

MAGE-1 #6

BAGE #1

A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S GCCGCTATGGCTGCAGGCCAGACTGATGAAGGAAGAGTCCCCCGTCGTGTCC

PRAME #34

T F Y D P B P I L C P C F M P N A A ACCTITIACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

MAGE-3 #12

I B L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT

GAGB-1 #2

TRP2IN2 #2

E A G G F F P W L K V Y Y Y R F V I G L R V W Q W E V I S C GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT

PRAME #1

A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E GCCGCTATGGAAAGGAGGAGGATCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA

TRP2IN2 #1

A A L M B T H L S S K R Y T B E A G G P P P W L K V Y Y Y R GCCGCTCTGATGGAGACACCTCCAAGGATACACAGGGGAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA

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MAGE-1 #1

A A M S L E Q R S L H C K P E E A L B A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGAGCCTCCACTGTAGGCTGAGGAAGAGGCTCTGGGACTGGGTCTGCGTC

MAGE-1 #3

Q A A T S S S S P L V L G T L B E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCCCCTCGTGCTCGCACACGCTCCCCCACAGGCCCCACAGCCCCCCACAGCCCCCCACAGCCCTCCCCCAAAGCCCT

PRAME #4

A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCCTGCCTAGGGAACCCTCAAGGCTATGGTC

MAGE-3 #16

E L S V L E V P E G R E D S I L G D P K K L L T Q H F V Q E GAGCTCAGCGTCCTGGAAGTGTTTGGGGGAAGGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA

MAGE-1 #11

ESLQLVFGIDVKEADDPTGHSYVLVTCLGGLGGCTGCCCTGCCTGCTCCTGCTCCTGCTCTCTGGGACTGTCCCGGCCTCCTGCGGACTGTCTCGGACTGTCCTGCGGACTGTCCTGCGGACTGTCCTGCGGACTGTCCCTGCTGGGACTGTCCC

MAGR-3 #5

PDPPQSPQGASSLPTTMNYPLWSQSYEDSSCCCGATCCCCCTCAGTCCCCCCCAAGGCGCTAGCTCCCCTGCCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC

LAGE1 #1

NYNSOla #12

Q C F L P V F L A Q P P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAAGGGCTGCC

gp100In4 #2

TWGBGLPSQPIIHTCVYFFLPDHLSPGRPFACCTGGGGGGGAGGCCTCCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT

MAGE-1 #7

S T S C I L E S L P R A V I T K K V A D L V G F L L L K Y R AGCACAAGCTCTCTCCTCGAGTCCCTGTATACCGAAAAAGGTCGCCGATCTGGTCGCCTTTCTGCTCCTGAAATACAGA

NYNSOla #1

GAGE-1 #7

D G P D G Q E M D P P N P E B V K T P E B B M R S H Y V A Q GACGGACCCGAAGACGCCAAGACGCAAGAGGCAATGACAAGCCATTACGTCGCCCAA

NYNSOla #11

ISSCLQQLSLLMWITQCFLPVFLAQPPSGQATCTCCCAGCTGTCTCTGCCTGGCTCAGCCTCCCTCCGGCCAA

PRAME #26

MAGE-3 #17

L G D P K K L L T Q H P V Q E N Y L B Y R Q V P G S D P A C CTGGGGAGACCTTAGAGAAACTGCTCACCAACACTTTTGGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCTGCTGT

MAGR-1 #:

NYNSOla #7

NYNSO1b #4

E E A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC

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BAGE #3

W R L B P B D G T A L C F I F A A TGGGGACCGGAACCGGAGACCGCTCTGTGTTCATTTTCGCTGCC

GAGE-1 #3

E Q F S D E V E P A T P E E G E P A T Q R Q D P A A A Q E G GAGCAATTCTCCGACGAAGTGGAACCCCCTACCCCTACGGAAGGCGAACCCCGCTACCCCAAGAGGGA

MAGR-3 #6

T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTAGGAAGACTCCAGGAAGAGGAGGAGGGCCCTAGGACATTCCCTGACCTCGAGTCC

MAGE-3 #

NQEEEGPSTFPDLESEFQAALSRKVAELVH AACCAAGAGGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAAATCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT

PRAMB #13

V D L F L K B G A C D B L P S Y L I B K V K R K K N V L R L GTGGATCTGTTCTGAAGAGGGAGAGGCTGTGAGAACTGTTTAGCTAGTTGAGAAAGTGAAAAGGAAAAGAATGTGCTCAGGCTC

NYNSOla #10

MAGE-3 #1

A A M P L B Q R S Q H C K P E B G L B A R G B A L G L V G A GCCCTATGCCTCTGGAACAGAGAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCAGAGGCTTGGGAACAGGCTCTGGGAGCTAGGCGAGGCTCTGGGAGCTTGGGCGCCT

NYNSOla #2

DADGPGGPGIPDGPGNAGGPGBAGATGCCGAGGCAAACGCTGGCGGACCCGGAGAGGCTGCCGTGCCGAGGCAGA

MAGE-3 #19

Y B F L W G P R A L V B T S Y V K V L H H M V K I S G G P H TACGAATTCCTCTGGGGGACCCCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT

PRAMB #23

MAGR-3 #18

N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT

MAGE-3 #11

VIPSKASSSLQLVFGIELMBVDPIGHLYIP GTGATTTTCTCCAAGGCTGGGCCTCCAGCTCCAGCTCGTGTTTGGCCATTGGACTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT

PRAME #21

PRAME #20

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGGGGAAGGCTC

PRAME #7

G Q H L H L B T F K A V L D G L D V L L A Q B V R P R R W K
GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCAAGAGGCTCAGGACATTGAAA

TACR1 #10

FIRLTAADHRQLQLSISSCLQQLSLLMWITTTCATTAGGCTCACCGCTGCCGGATCACGACAGCACCGCTCAGGCTCCAGGCTCCAGCATCACGACCTCCAGCACCACCAGCAACTGTCCCTGCCTCATGTGGATCACA

PRAME #15

C C K K L K I P A M P M Q D I K M I L K M V Q L D S I B D L
TGCTGTAAGAAACTGAAAATCTTTGCCATGCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC

NYNSO1a #5

GAPRGPHGGAASGLNGCCRCGARGGGGCCCGAAAGCAGACTGCTCCCAGAGGCCCTCACGGAGCCCTCCACGGCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC

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MAGE-1 #8

KKVADLVGFLLLKYRAREPVTKAEMLESVI AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGACTCAGTATGGGGTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT

MAGB-1 #13

PRAME #2

S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L B S Y AGCATTAGCGCTCTGCAAAGCCTCATCGGAAAGCTAT

MAGE-3 #15

I A R E G D C A P E E K I W B E L S V L E V P E G R E D S I ATCCCTAGGGAAGGCGATTGCCTCCCGAAGAGAAATCTGGGAGGAACTGTCCGTGCTCGAGGGTCTTCGAAGGCAGAGGATAGCATT

PRAME #22

D Q L L R H V M N P L E T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTTGCAGACTGTCCGAGGGGAGACGTCATGCATCTGTCC

MAGE-1 #19

PRAME #30

S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACACGTCCTGTATCCCGTCCCCTCGAGGTCCTTACGGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC

NYNSO1b #1

MAGE-1 #10

KNYKHCFPEIFGKASBSLQLVFGIDVKBAD

MAGE-3 #4

PRAME #32

HARLRBLLCELGRPSMVWLSANPCPHCGDR CACGCTAGGCTCAGGGAACTGCGAACTGGGAAGGCCTAGCATGCTGTGCCCATTCCGGAGACAGA

PRAME #25

GAGR-1 #9

E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E GAGGATGAGGGAGCCTCCCCGAACCCGAACCCGAACCCGAACCCGAAGCCAAGGCCAAGGCCATCCCCAAACCCGGATGCGAA

MAGE-3 #10

E M L G S V V G N W Q Y P F P V I F S K A S S S L Q L V F G GAGATGCTGGGAAGCGTCGTGGGAAACTGGTCTTCCGGAAGCCTCCAGCTCCTGCAACTGGTCTTCGGA

GAGE-1 #1

A A M S W R G R S T Y R P R P R R Y V E P P B M I G P M R P GCCGCTATGTCCTGGGAGGCAGAGGCACACAGACCCAGAGGCTATGTGGAACCCCTGAGATGATGGACCCATGAGGCCT

PRAME #2

Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A
TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGGCTCCTGGCAGGGTCGCCTAAGGATGAGGCTCTGGCTATCGCT

MAGE-1 #16

Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGGCAGAGAGCATAGGCTTACGGAGAGCCTAGGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA

LAGB1 #12

Q C F L P V F L A Q A P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGCTGCC

PCT/AU01/00622 WO 01/090197

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MAGE-3 #20

V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA

Q L H I T M P P S S P M E A B L V R R I L S R D A A P L P R CAGCTCCACATTACCATGCCCTTTAGCTCCCCCATGGAGGCTGAGCTCGTGAGAAGGATTCTGTCCAGGGATGCCGCTCCCCCCAGA

PGVLLKEPTVSGNILTIRLTAADHRQLQLS CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCCAACTGTCC

PRAME#16
KMILKMVQLDSIEDLEVTCTWKLPTLAKFS AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC

F L I I V L V M I A M E G G H A P E E E I W E B L S V M E V TTCCTCATCATTGTGCTCGTGATGGTCGCTATGGAAGGCGGACACGCTCCCGAAGAGGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTC

B V T C T W K L P T L A K P S P Y L G Q M I N L R R L L L S GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC

E G L E A R G E A L G L V G A Q A P A T E E Q E A A S S S S GAGGGACTGGAAGCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC

MAGE-3 #21

I SYPPLHEWVLREGEEAA 

HIHASSYISPEKEEQYIAQFTSQFLSLQCL CACATTCACGCTAGGTCCTACATTAGCCCTGAGAAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC

G N A G G P G B A G A T G G R G P R G A G A A R A S G P G G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGGCGTGCCGCTGCCAGAGCCTCCGGCCCTTGGCGGA

G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGCTAGGGCTAGCGGACCCGGAGGCGGAGCCCCTAGGGGAGCCCCATGGCGGAGCCCCTAGCGGACTGAAT

Q G A S A F P T T I N F T R Q R Q P S E G S S S R E E E G P 

NYNSOla #8

LARRSLAQDAPPLPVPGVLLKBFTVSGNIL 

A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTTGGGAGTGCTCATGAAA

MAGE-1 #20

I K V S A R V R F F F P S L R E A A L R E B B B G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGAAGAGGAAGGCGTCGCCGCT

G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCGCCCTCCTGCCTAGCCTCAGCCATTGCTCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT

V K T P B B B M R S H Y V A Q T G I L W L L M N N C P L N L GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC

ISSCLQQLSLL M W I T Q C F L P V P L A Q A P S G Q 

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PRAME #14

Y L I'E K V K R K K N V L R L C C K K L K I F A M P M Q D I
TACCTCATCGAAAAGGTCAAGAGAAAAGAAAAACGTCCTGAGACTGTGTGCAAAAAGCTCAAGATTTTCGCTATGCCTATGCAAGACATT

MAGE-1 #9

A R B P V T K A E M L B S V I K N Y K H C F P B I F G K A S GCCAGAGAGCCTGTGACAAAGGCTGGAGAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC

LAGE1 #8

L V R R I L S R D A A P L P R P G A V L K D F T V S G N L L CTGGTCAGGAGAATCCTCAGCAGAGACCCTCTGCCCTCTGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC

PRAME #2

H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGACCACCTCCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGCTCCAGCACTCCAGCACTGATTGGCCTC

PRAME #33

M V W L S A N P C P H C G D R T F Y D P B P I L C P C F M P ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTTATCCCCTTGCCCTTTATGCCCT

gp100In4 #1

A A S W S Q K R S F V Y V W K T W G B G L P S Q P I I H T C GCCGCTAGCTGGGAGGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAAGGGACTGCCTAGCCAACCCATTATCCATACCTGT

BAGE #2

L L Q A R L M K E E S P V V S W R L B P B D G T A L C F I F CTGCTCCAGGCTAGGCTCAGGCTCAGCCTCTGCTTATCTTT CTGCTCCAGGCTCAGGCTCAGGCTCAGGCTCAGGCTCAGCCCTCTGCTTTATCTTT

gp100In4 #3

V Y F F L P D H L S F G R P F H L N F C D F L A A GTGTATTTCTTTCTGCCTGACCATCTGCCTCCCCGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC

PRAME #18

MAGE-3 #3

PRAME #6

Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGGCCTTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA

PRAME #12

NYNSO1b #3

A E V P G A Q G Q Q G P R G R E E A P R G V R M A A R L Q G GCCGAAGTGCCTGGGGCTCAGGGCCTCAGGGCCTCAGGGCACGCCCTAGGCTCCAGGGA

LAGB1 #5

G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L
GGCGCTCCCAGAGGCCCTCACGGAGGCGCTCCCCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC

LAGE1 #4

G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGCTAGGGCTAGGGCTCAGGGCCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGGACCCCCTAGGGCTCAGGGTCAGGAT

PRAME #3

LAGQSLLKDEALAIAALELLPRELPPLFM
CTGGCTGGCCAAAGCCTCTGAAAGACCCTCTCGCCATTGCCGCTCTGGAACTGCTCCCCAGAGAGCTCTTCCCCCCCTCTTCATG

GAGE-1 #4

BPATQRQDPAAAQBGBDBGASAGQGPKPEAGGCCTGCCGCCACGCACGCCCTAGGCCCTGAGGCCTGAGGCCTGAGGCCTGAGGCCTAGGCCTGAGGCCTTAGGCTTGAGGCT

PRAME #11

PEAAQPMTKKRKVDGLSTEAEQPFIPVEVL

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LAGE1 #6

G R C P C G A R R P D S R L L Q L H I T M P F S S P M E A E GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA

P G A V L K D F T V S G N L L F I R L T A A D H R O L O L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC

PRAME #31

EDIHGTLHLERLAYLHARLRELLCELGRPS GAGGATATCCATGGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCC

D S Q B Q G H P Q T G C B C B D G P D G Q B M D P P N P B B GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA

F V I G L R V W Q W E V I S C K L I K R A T T R Q P A A TTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCT

D A D G P G G P G I P D G P G G N A G G P G B A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA

PTGHSYVLVTCLGLSYDGLLGDNQIMPKTG CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA

P L L L K Y R A R E P V T K A E M L G S V V G N W Q Y P P P TTCCTCCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTCGGCAATTGGCAATACTTTTTCCCT

T G I L W L L M N N C P L N L S P R K P A A ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT

MAGE-3 #8

E F Q A A L S R K V A E L V H F L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT

V P D S D P A R Y E F L W G P R A L A E T S Y V K V L E Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC

NYNSOla #6

G C C R C G A R G P E S R L L B F Y L A M P F A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA

A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT

G N A G G P G B A G A T G G R G P R G A G A A R A S G P R G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGCGTGCCAGAGCCTCCGGCCCTAGGGGA

Artificial Protein:

APBEBIWERLSVMBVYDGRBHSAYGBPRKLEBVPTAGSTDPPQSPQGASAFPTTINFTRQTVWSGNRASLYSPPEPBAAQPMTKKRKVDGOIMPKAGL LIIVLAIIAREGDCAPBEKIWELQVLDLRKNSHQDPWTVWSGNRASLYSFPELDVLLAQEVRPRRWKLQVLDLRKNSHQDPWQGAMLAAQERRVPRAA evpgaqgqqppgrqspsvsqlsvlslsgvmltdvspeplqallltqdlvqekyleyrqvpdsdparyeplmgprqpsegsssreeegpstscilesl FRAVITAAMAARAVPLALSAQLLQARLMKBESPVVSTFYDPEPILCPCFMPNAAIELMEVDPIGHLYI FATCIGLSYDGLLGDNRRYVEPPEMIGPMR PEQFSDEVEPATPEEGEAGGFPPWLKVYYYRPVIGLRVWQWEVISCAAMERRRLMGSIQSRYISMSVWTS PRRLVEAALMETHLSSKRYTEEAGGFPP WLKVYYYRAAMSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPOSPALELLPRELFPPLFMAAFDGRHSOTLKAMV ELSVLEVFBGREDSILGDPKKLLTQHFVQBBSLQLVFGIDVKBADPTGHSYVLVTCLGLSPDPPQSPQGASSLPTTMYYPLWSQSYBDSSAMQABGQ GTGGSTGDADGPGGPGIPDGPGQCPLPVFLAQPPSGQRRAATWGBGLPSQPIIHTCVYPFLPDHLSFGRPFSTSCILRSLPRAVITKKVADLVGFLLL KYRAAMQABGRGTGGSTGDADGPGGPGIPDGPGDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQISSCIQQLSLLMWITQCFLPVFLAQPPSGQERASA TLQDLVFDBCGITDDQLLALLPSLSLGDPKKLLTQHPVQENYLEYRQVPGSDPACEALBAQQEALGLVCVQAATSSSSPLVLGTLEFYLAMPPATPME aelarrslagdapplpvbeaprgvrmaarlqgaawrlepedgtalcp1faaeqfsdevepatpeegepatqrqdpaaaqegtmnyplwsqsyedssnq EEEGPSTPPDLESNQEEEGPSTPPDLESEFQAALSRKVAELVHVDLFLKEGACDELPSYLIEKVKRKKNVLRLTIRLTAADHRQLQLSISSCLOOLSL LMWITAAMPLEQRSQHCKPEEGLBARGEALGLVGADADGPGGPGIPDGPGGNAGGPGBAGATGGRYEFLWGPRALVETSYVKVLHHMVKISGGPHITN CRLSEGDVMHLSQSPSVSQLSVLSLSGNYLEYRQVPGSDPACYEPLWGPRALVETSYVIFSKASSSLQLVFGIBLMEVDPIGHLYIPQALYVDSLFFL

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RGRLDQLLRHVMNPLETLSYLAQFTSQFLSLQCLQALYVDSLPFLRGRLGQHLHLETFKAVLDGLDVLLAQEVRPRRWKFIRLTAADHRQLQLSISSCLQQLSLLMWITCCKKLRIFAMPMQDIKMILKMVQLDSIKDLGAPRGPHGGAASGLNGCCRCGARGPESRLLKKVADLVGFLLLKYRAREPVTKAEMLE SVIYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHSISALQSLLQHLIGLSNLTHVLYPVPLESYIAREGDCAPEEKIMEELSVLEVFEGREDSIDQLLR hvmnpletlsitncrlsegdvmhlsralaetsyvkvleyvikvsarvrfffpslrsnlthvlypvplesyedihgtlhlerlaylaamlmaqealafl Maqgamlaaqerrvpraknykhcppeipgkaseslqlvpgidvkbadtlvbvtlgbvpaabspdppqspqgasslptharlrellcblgrpsmvmlsa npcphcgdrvmltdvspeplqallerasatlqdlvfdecedegasagqgpkpradsqeqchpqtgcecremlgsvvgnwqypfpv1fskassslqlvf GAAMSWRGRSTYRPRPRRYVEPPEMIGPMRPYISMSVWTSPRRLVELAGQSLLKDEALAIAYDGREHSAYGEPRKLLTQDLVQEKYLEYRQQCFLFVF LAQAPSGQRRAAVKVLHHMVKISGGPHISYPPLHEWVLREGEQLHITMPPSSPMEAELVRRILSRDAAPLPRPGVLLKEFTVSGNILTIRLTAADHRQ lolskmilkmvoldsiedlevtctwklptlakpspliivlvmiamegghapeeeiweelsvmevevtctwklptlakpspylgominlrrlllsegle argealglygaqapateeqeaassssisypplhewvlregebaahihassyispekeeqyiaqptsqplslqclgnaggpgeagatggrgprgagaar asgpggprgagaarasgpgggaprgphggaasglnqgasappttinftrqrqpsbgsssreebgplarrslaqdapplpvpgvllkeptvsgnilaa PDGRHSQTLKAMVQAWPFTCLPLGVLMKIKVSARVRFFPPSLRRAALREEEEGVAAGITDDQLLALLPSLSHCSQLTTLSFYGNSIVKTPEEEMRSHY VAOTGILWILLMINCPLINLISSCLQQLSLLMWITQCFLPVFLAQAPSGQYLIEKVKRKKNVLRLCCKKLKIPAMPMQDIAREPVTKAEMLESVIKNYKH CFPBIFGKASLVRRILSRDAAPLPRPGAVLKDFTVSGNLLHCSQLTTLSFYGNSISISALQSLLQHLIGLMVWLSANPCPHCGDRTFYDPEPILCPCF mpaasmsqkrsfvyvwktmgeglpsqp1ihtcllqarlmkbespvvswrlbpedgtalcf1fvyfflpdhlsfgrpfhlnpcdflaapylgqminlrr lllshihassyispekebqqapatebqbaasssstlvbvtlgevpaabsqawpftclplgvlmkgqhlhletpkavldglstraeqpfipvbvlvdlf  ${\tt LKEGACDELPSAEVPGAQGQQGPRGREEAPRGVRMAARLQGGAPRGPHGGAASAQDGRCPCGARRPDSRLLGPRGAGARASGPRGGAPRGPHGGAAS}$ aqdlagqsllkdeala1aalellprelppelpmepatqrqdpaaaqegedegasagqgpkpeapeaaqpmtkkrkvdglsteaeqppipvevlgrcpc GARRPDSRLLQLHITMPFSSPMEAEPGAVLKDFTVSGNLLFIRLTAADHRQLQLSEDIHGTLHLERLAYLHARLRELLCELGRPSDSQEQGHPQTGCE CEDGPDGQEMDPPNPEEFVIGLRVWQWEVISCKLIKRATTRQPAADADGPGGPGIPDGPGGNAGGPGBAGATGGRPTGHSYVLVTCLGLSYDGLLGDN QIMPKTGPLLLKYRAREPVTKABMLGSVVGNWQYFFPTGILWLLMNNCFLNLSPRKPAABPQAALSRKVABLVHPLLLKYRAREPVTKAVPDSDPARY eflwgpralaetsyvkvlbyvgccrcgargpbsrllefylamppatpwrabatclglsydgllgdnqimpkaglliivlaignaggpgbagatggrgp RGAGAARASGPRG

### Artificial DNA:

GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCCAGAAAGCTCGAGGAAGT ATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAGATCGACGGACAGATTATGCCTAAGGCTGGCCTC CCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAACTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGT GGAAGCTCCAGGTCCTGGATCTGAGAAAGAATAGCCATCAGGATTTCTGGCAGGGAGCCATGCTGCCCCAAGAGAGAAGGGTCCCCAGAGCCGCT TTCAGAGCCGTCATCACAGCCGCTATGGCTGCCAGAGCCGTCTTCCTCGCCCTCAGCGCTCAGCTCAGCCAGACTGATGAAGGAGGAGGAGTCCCC  $\tt CGTCGTGTCCACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCTATCGAACTGATGGGGGTCGACCCTATCGGACACCCTATCGGACACCCTATCGGACACCCTATCGGACACCCTATCGGACACCCCTATCGACACCCCTATCCCCCAATGCCCCCAATGCCCCCAATGCCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCCAATGCCCAATGCCCCAATGCCCCAATGCCCAATGC$ TCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAATAGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGA CCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGGGAGGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGT GATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGTGCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGT CCGTGTGGACCTCCCCAGAAGGCTCGTGGAAGCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCT TGGCTCAAGGTCTACTATTACAGAGCCGCTATGTCCCTGGAACAGGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGACGCTCAGCAAGAGGCTCT GGGACTGGTCTGCGTCCAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCC AAAGCCCTGCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAAGAGTCCCT gcaactggtcttcggaatcgatgtgaagggggggccctaccggacactcctacgtcctggtcacctgtctggactgtcccccgatccccctcagt CCCCCAAGGCGCTAGCTCCCTGCCTGCCACAAGGATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCCGCCGCTATGCAAGCCAAAGGCCAA GGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGACAGTGTTTCCTCCCCGTCTTCCTCGCCCAACC CCCTAGCGGACAGAGAGGGCTGCCACCTGGGGCGAAGGCCTCCCCTCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCGGATCACCTCA GCTTTGGCAGACCCTTTAGCACAAGCTGTTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTG AAATACAGAGCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGCCGTTATGCAGGACCCGGAATCCCTGACGGACCCGG AGACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGGAAATGAGAAGCCATTACGTCGCCCAAATCTCCA ACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCCTGCTCCCTGTCCCTGGGAGACCCTAAGAAACTGCT CACCCAACACTTTGTGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCCTGTGAGGCTCTGGAAGCCCAACAGGAAGCCCTCG GCCTCGTGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTCTGGTCCTGGGAACCCTCGAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAG GCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTCGAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGC TGCCTGGAGACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCCGAGCAATTCTCCCGACGAAGTGGAACCCGCTACCCCTGAGGAAG GCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGAACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAG TCTGTCCAGGAAAGTGGCTGGGCTCGTGCATGTGGATCTGTTTCTGAAAGAGGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAAGTGAAAA CTCATGTGGATCACAGCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGT ACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGGGGACCCCATATCACAAAC TGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTTAGCGTCAGCCTAACTGTCCGTGCTCAGCCTCAGCGGAAACTATCTGGAATACAG ACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTATGTGATTTTCTCCAAGGCTAGCTCCA AGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCCTACATTGCCCAATTCACAAAGCCAATTCCTCAGCCTCCAGTG TCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTCGGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCG CTCCAGCAACTGTCCCTGCTCATGTGGATCACATGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGT

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CCAGCTCGACTCCATCGAAGACCTCGGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGGCCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGAC CCGAAAGCAGACTGCTCAAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAG TAGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGCCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTTATCGCTA  ${\tt GGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATTGACCAACTGCTCAGG$ CATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCCAGGGCTCTGGCTGAGACAAGCTA ATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGGGCCTAGGGCTAAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGGGA AAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGATACCCTCGTGGAAGTGACACTGGGAGAGGGTCCCCGCTGCCGAAAGCCCTGACCCTC AATCCCTGTCCCCATTGCGGAGACAGAGTGATGCTGACAGACGTCAGCCCTGGGCCTTGCCAGGACCCTCCTGGAAAGGGCTAGCCCTACCCTCCAGGA TCTGGTCTTCGATGAGTGTGAGGAGGGGGGGCCCTCCGCCGGACAGGGGCCCAAACCCGAAGCCCAAGGCCAAGGGCCATCCCCAAACCGGAT GGAGCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAAGGTATGTGGAACCCCTGAGATGATGGACCCATGAGGCCTTACAT TAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCTTACGATGGCAGAG AGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAACAGTGTTTCCTCCCCGTCTTC GCATGAGTGGGTGCTCAGGGAAGGCGAACAGCTCCACATTACCATGCCCTTTAGCTCCCCCATGGAGGCTCAGTGAGAAGGATTCTGTCCAGGG ATGCCGCTCCCCTCGCGAGACCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAA CTGCAACTGTCCAAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAACT CTCCTTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGGCGGACACGCTCCCGAAGAGAGAATCTGGGAGGAACTGTCCGTGATGGAGGTCGAGG TCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCCGAGGGACTGGAA  ${\tt CGAATGGGTCCTGAGAGAGGGAAGGCGCTCACATTCACGCTCAGCTCCTACATTAGCCCTGAGAAAGAGGGAACAGTATATCGCTCAGTTTACCT}$ CCCAGTTTCTGTCCCTGCAATGCCTCGGCAATGCCGGAGGCCCTGGCGAAGCCGGAGGCCACAGAGGGGGAAGCCAGAGGCGCCTGCCAGA GCCTCCGGCCCTGGCGGAGGCCCTAGGGGAGCCGGAGCCGTAGGGGTAGCGGACCCGGAGGCGGAGCCCCTAGGGGGACCCCATGGCGGAGCCGCTAG CTCTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTCAAGGAATTCACAGTGTCCGGCAATATCCTCGCCGCT TTCGATGGCAGACACTCCCAGACACTGAAAAGCCATGGTGCAAGCCTTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAAATCAAAGTGTCCGC TCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATTGTGAAAACCCCTGAGGAAGAGATGAGGTCCCCACTAT GTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTCATCTCCAGCTGTCTGCAACAGCTCAGCCTCCTGATGTGGATTAC aaaagctcaagattittcgctatgcctatgccaagacattgccagagagcctgtgacaaaggctgagatgctggaaagcgtcatcaaaaactaataagcat TGCTTTCCCGAAATCTTTGGCAAAGCCTCCCTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTT CACAGTGTCCGGCAATCTGCTCCACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCAGCCCTCCAGTCCCTGCTCCAGC ATCTGATTGGCCTCATGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTT ATGCCTGCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGTCT GCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGGCTGAGGATGGCACAGCCCTCTGCTTTATCTTTTGTGTATTTCT TTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCCCCCTATCTGGGACAGATGATCAATCTGAGAAGG CTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAAGCAACAGGCTCCCGCTACCGAAGAGCAAGAGCTGCCTCCAGCTC AGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGACTGTCCACCGAAGCCGAACAGCCTTTCATTCCCGTCGAGGTCCTGGTCGACCTCTTC CCGATAGCAGACTGCTCGGCCCTAGGGGAGCCGGAGCCGCTAGGGGTAGCGGAGCCCAGAGGCGGAGCCCCATGGCGGAGCCCCATGGCGGAGCCGCTAGC GGAGCCTGCCACACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTGAGGCCCTAAGCCTGAGGCTCCCGAAG CCGCTCAGCCTATGACAAAGAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTCGGCAGATGCCCTTGC GGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCCCAGCCCTATGGAAGCCCGAACCCGGAGCCGTCCTGAAAGACTT TACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCCGAGGATATCCATGGCACTGCATCTGCAAA GGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCCGACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAG TGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAATTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAA ACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCTGGCGGAAACGCTGGCGGAC CCGGAGAGGCTGCCGTACCGGAGGCCAGACCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAAC ATACTTTTTCCCTACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCTGAGTTTCAGGCTGCCCTCA GCAGAAAGGTCGCCGAACTGGTCCACTTTTCTGCTCCTGAAATACAGAGGCCAGAGAGCCTGTGACAAAAGGCTGTGCCTGACTCCGACCCTGCCAGATAC GAATTCCTCTGGGGACCCAGAGCCCTCGCGGAAACCTCCTACGTCAAGGTCCTGGAATACGTCGGCTGTTGCAGATGCGGAGCCCAGAGGCCCTGAGTC CAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAAGCCACATGCCTCGGCCTATGACGGACTGCTCGGCCGATA ACCARATCATGCCCARAGCCGGACTGCTCATCATTGTGCTCGCCATTGGCAATGCCGGAGGCCCTGGCGAGCCGGAGCCACAGGCGGAAGGGGAACCC AGAGGCGCTGGCGCGCGCGCCCTAGGGGA

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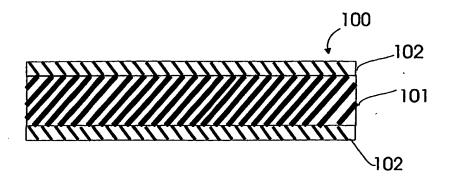


FIGURE 28

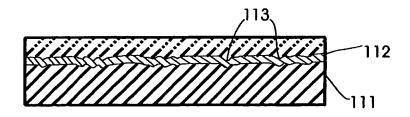


FIGURE 29

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# Cassettes for construction of a full-length HIV Savine

#### Cassette A1

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCACCGTGCAATGCACACACGGAATCAGACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAGAAGCCTCTACAATACCGTCGCCACACTGTGGTGCGTCCACCAAAGGAT TGACGTCAGGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCTTCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAAAGAATC CCGATATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTCTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGCAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAAGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGAAGTGAAAGATACCAAAGAGGCTTTGGATAA GATTGAGGAGGTGCAAAAGAAAAGCGAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCACTA  ${\tt CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGAGACAGAGGTCCACAATGTGTGGGCCACACGCTTGCGT}$ CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAAATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGGACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAGTTAGGATTATCAATATCCTTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCTCCAGGCAAACCAGAAAGAATAGGAGAAGGAGATGGGGAGGCGAACGGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAACCTCTGCCTCTTCGAAAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTGCCACAACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGAAGCGGCGCACAGACGAAGAGCTCCTGAGGGCTATCAGAATCATTAACATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAGAATCAGAACCTGGAACAGCCTGGTCAAGCATCACATGCACATCTCCA AGAAAGCCAAAGGCTGGTTCTATAGGCATCACTTTGAGGAGCTCGAGCTCGTGAATCAGATTATCGAAAAGCTCAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACAAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCTTTG TCTGAAACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCAGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA: GAGCAAAAGGATAAGGAGCAATACGATCAGATTCTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACGGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC AAAGGTCTCGGCATTAGCCACGGAAGGAAAAAGAGAAAACAGAGAGGGGAGCTCCCCAAGCTGCCATGGACCCCG TGGACCCCAAGCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTTACAAATGCTATTGCAAAAA GTGCCCTAGCGAAGAGACACCCCTAGCCAGAAACAGGAACAGAAGAACTCTACCCCCCTTTAGCCAGC CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATGACATGGTGGAACAGATGCAAGAAGACATTA TCTTACTATGGGACCAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGG

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AGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGAACACCTCCTGAAATGGGGACTCACCGAAACCACAAA CAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCATCTGCTCAAATGGGGCTTCACAACCCCTGACAAAAA AAGAGACGCAGAGAAAATCACACAATGAATGGCCATACTGCCACAGAGTCCCAGAATCAGCAAGACAGAAACGAAA AGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTAACATTACCGACACCGGAAATAGCTCCAA AGTGTCCCAGAATTACCCTATCGTCCAGAATGTCCAAGGCCAAATGGTCCACCAACCCCTCTCCCCCAGACTCATC GGACTGAGAATCGTTTTCGCTGTGCTCAGCATTATCAATAGGGTCAGGCAAGGCTATAGCCCTCTGTCCTTCCAAA CCCTCCCCTCATCCATCTGCAATACTTTGACTGTTTCGCTGACTCCACCATTAGGAGAGCCATCTTGGGACACAT AGTGAGAAGGAGATGCGAATACGCTGTGGGACTCGGAGCCATGTTCCTTGGCTTTCTGGGTGCCCGCTGGCTCCACC ATGGGCGCTGCCTCCATGACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCATTGCTGAGATTCAGAAAC AGGGCCAGGGTCAGTGGACATTTCAGATTTTCCAAGAGCCTTTCAAAAACGGAACCGTCCTGGTCGGCCCTACACC CGTCAACATCATCGGAAGGAACATGCTGACACAGCTTGGCCGCACTCTCAACTTTCCCATTAGCAAAGGCAGCCCT GCTATCTTTCAGTCCAGCATGCCACAGATTCTGGAGCCTTTTAGGATAAAAAACCCTGAGATGGTCATCTATCAGT ATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGCGAAGTGGAAGAGATCAACAA GGGCGAAAACAATTGCCCCCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCATCAATAACGAAACCCCTGGC ATTAGGTATCAGTATAACGTCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATGACCCTCACCGTCC AGGCTAGGCTACTGCTCAGCGGAATCGTCCAGCAACAGAGCAATCTGCTGGAGGAGAATAGGGAAATCCTCAGAGA GCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGGTCGCTGAAATCCAAAAGCAAGGCAGAGGAACTG TCCACCATGGTGGATATGGGAAACTACGACCTCGGAGTGGACAATAACCTCGCCGCTATTAGAATCCTGCAACAGC TCATGTTCATTCACTTTAGGATTGGCTGCCAGCACTCCAGGATTGGCATCATCCGTCAGAGAGGAGGGCCAGAGCTCC CAGGAAAAAGGGATGCTGGAAGTGTGGCAGAGAGGGCACACCAGATGAAGGATTGCACTGAGAGACAGGCTAACTTT ATGGCGTCAGCATTGAGTGGAGGATAAGGGAAAGGGCTGAGGATAGCGGCAACGAAAGCGAAGGCGACACAGAAGA GCTCAGCACATTGGTGGACATGGGCAATTACGATCTGTCTAGCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGA ATCGAAGAGGAGGCGGAGAGCAAGGCAGAGGCGCAGAGGCTCGGGAATGGCAGAGAGGTCGAGGAAGTCA GTGGCCAGCTTCTCTCCGAGCAAACAGGGGCTAACTCCTCTACAAGCAGAAAGCTGGGAGACGGAGGCGGAGCCG ACAGACAGGAACAAGCTCCAGCTGTTTCAATTGCGGCAAAGAGGGGACACATTGCCAAAAACTGTAGGGCCCCTCG CAAGAAAGGTTGTTGGAAATGCGGAAAGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTC GGCAAAATCTGGCCCTCCAACAAAGGCAGACCCGGAAACTTTCTCCAAAGCAAATGGCTCTGGTATATCAAAAATCT TTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATCTTTGCCGTCCTGTCCATCGTTAACGGAGCCGTGAG CCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATACCGCTGCCAATAACGCTGACTGTGTCTGGCTGAAG GCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGCCTTTATCGTCGCCCTCATCATAGCCATTGTGGTCT GGACAATCGTCTACATTGAGTATGTCGACtqaaqatctqaattc

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### A2 fragment

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCTCCGTGCAATGCACACAGGAATCAAACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAAAAGCCTCTACAATACCGTCGCCACACTGTGGTGTGTCCACCAAAGGAT TGAGGTCAAGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCATCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAGAGAATC CCGAAATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTTTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGAAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAGGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGATGTGAGAGATACCAAAGAGGCTCTGGATAA GATTGAGGAGGAGCAAAACAAAAGCAAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCCATTCAAGAAGCCGATA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGACACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAGATCGGACCCGAAAACCCTTACAATACCCCCAATCTTCGCTATCAAGAAAAAGAACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAATTAGGATTATCAAAATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCACCAGGCAAACCAGAAAGAATAGGAGAAGGGGGATGGGGAGCGGAACAGGGTAGGGTAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGGCACGACCTCTGGGACGACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGGGCTAACACACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGCAGCAGCAGACGAAGACGTCCTGAAGGCTGTCAGAATCATTAAGATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAAAATCAGAACCTGGAAGAGCCTGGTCAAGCATCACATGTACATCTCCA AGAAAGCCAATGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGGTCGTGAATCAGATTATCGAAAAGCTTAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGGAATCGGACGAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCCTTG TCTGAGACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCGGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCCAAAGGATAAGGAGCAATACGATCAGATTATTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC TGGACCCCAACCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTAACAAATGCTATTGCAAAAA GTGCCCTAGCGAAGAGACACCCCTAGCCAGAAACAGGAACAGAAAGACAAGAACTCTACCCCCCTTTAGCCAGC CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATAACATGGTGGAACAGATGCAAGAAGACATTA TCTCACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGCA

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CACCTCCTGAGATGGGGACTCACCGACACCACAAACCAAAAGACTGAGCTCCACGCTATCCATCTGGCTCTGCAAG ACTCCGGCTTAGAGGTCAACATTGTGACAGACATTCCCGCTGAGACTGGTCAAGAGACCACCTATTTCATTCTGAA ACTGGCTGGCAGATGGCCTGTGAGAATCATTCACACAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCAT CTGCTCAAATGGGGCTTCACAACCCCTGACAAAAAGCGTCAGAAAAGGCCTCCCTTTCTGTCTAGTGTCAAGAAAC CACAGAGTCCCAGAATCAGCAAGACAGAAACGAAAAGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAAT TGGTTTAACATTACCGACACCGGAAGTAGCTCCCAAGTGTCCCAGAATTACCCTATCGTCCAGAATCTCCAAGGCC AAATGGTCCACCAACCCATCTCCCCCAGACTCGTCGGACTGAGAATCATTTTCGCTGTGCTCAGCATTATCAATAG GACTCCACCATTAGGAGAGCCATCCTTGGACACAGAGTGAGCAGGAGATGCGAATACGCTGTGGGAATCGGAGCCA TGTTCCTTGGCTTTCTGGGTGCCGCTGGCTCCACCATGGGCGCTGCCTCCATCACACTGACAGTGCAAGCCTATGA  ${\tt CCCTAGCAAAGACCTCATTGCTGAGATTCAGAAACAGGGTCAGGATCAGTGGACATATCAGATTTTCCAAGAGCCT}$ GCACCCTCAACTTTCCCATTAGCAAAGGCAGCCCTGCTATCTTTCAGTCCAGCATGACACAGATTCTGGAGCCTTT TAGGAAACAAAACCCTGACATGGTCATCTATCAGTATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTC CCCGTGGACCCCAGCGAAGTGGAAGAGACCAACAAGGGCGAAAACAATTGCCTCCTGTTTAGGAAATACACAGCCT TTACCATTCCCTCCACCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAG CACAATGGGAGCCGCCAGCATGACCCTCACCGTCCAGGCTAGGCAACTGCTCCAGCGGAATCGTCCAGCAACAGAAC AATCTGCTGGAGGAGAATAGGGAAATCCTCAAAGAGCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGA TCGCTGAAATCCAAAAGCAAGGCACAGAGGAACTGTCCGCCTTGGTGGATATGGGAAACTACCACCTCGGAGTGGA ATTGGCATCATCCGTCAGAGAAGGGCCCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCAAAGAGGGACACC AGATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGATGCCAGACTGGTTATCAAAACCTATTGGGG ACTGCATACCGGTGAGAGAGCTGGCACCTCGGCCATGGCGTCAGCATTGAGTGGAGGACAAGGGAAAGGGCTGAG GATAGCGGCAACGAAAGCGAAGGCGACAGAGAAGAGCTCAGCACAATGGTGGACATGGGCAATTACGATCTGTCTA CAGGCTCGTGAATGGCAGTGAGGGCGAGGAAGTCAATAAGGGAGAAATAACTGTCTGCTCCACCCTATGAGTCAA CATGGCATGGAAGACGAAGACAGAGGGTCAATAGCGATATCAAAGTGGTCCCCAGAAGGAAAGCCAAAATCATTA GGGATTACGGAAAGCAAATGGCTGACGATGACTGTGTGGCCGGCTTCTCTCCGAGCAAACAAGGGGCTAACTCCCC TGCAAGCAGAAAGCTGGGAGACGGAGCCGACAGACAGGCAACAAGCTCCAGCTGTTTCAATTGCGGCAAA GAGGGACACATTGCCAAAAGCTGTAGGGCCCCTCGCAAGAAAGGTTGTTGGAAATGCGGAAGGGAAGGCCATCAAA TGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGGCAAAAATCTGGCCCTCCAAAAAAAGGCAGACCCGGAAACTT TCTCCAAAGCAAATGGCTCTGGTATATCAAAATCTTTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATC TTTGCCGTCCTGTCCATCATTAACGGGGCCGTGAGCCCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATA CCGCTGCCAATAACCCTGACTGTGTCTGGCTGGAGGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGC CCTTATCGTCGCCCTCATCATAGCCATTGTGGTCTGGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaa ttc

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### B1 fragment

qqatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGAGACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCACCTTTAGGCCTGGCGGAGGCAATATCAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGACCCTATCGTTGGCGTTGAGCCTCAGGATC CTCTGTCCTGTTTCTGGATGGCATTGACAAGCTCAAGAGGAACATGAAAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCAGCC TGTCAAAACCATTATCGTCCAACTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCTAGTGTCCTCAGAGGC GCCTGGAGGGACTGGTTTACTCCAAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCATGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGGGGGGGGAGACAGCTCCTGTCCGGCATTGTGCAACAACAAAATAACCTCCTGAGGGCTATCGAAG  $\tt CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACGGCCTGGGACAGTA$ CATCTATGAGACATACGGAGACACATGGGCGGGAGTGGAAGCCCTCACAGCCCTCATCACACCCCAAAAAGATTAGG CCTCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAGATGGAATGAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTATCGATATCATTGCATCCGACATTCAGACTAAGGAACTGCAAAAGCAAATCCTAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAATCATTGACATTATC GCCACCGATATCATTCCCGTGGGCGAAATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATCTACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGCTGCCCGC CCTCTGCCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAAGGCAAAAAAGGCTAGTGGAGGGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAACCGCTGTGCAAATGGC TGCCATGCAGATGCTCAAGGATACCATTAACGAAGAGGCTGCCGAGTGGGACAGAGTCCATCCCGTCCATGCCGGG CCCGTTCCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAAGATTGGCCCTGAGAATC CCTATAACACCCCATCTTTGCCATTCAAGTGAGAGAGCCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTTGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAATCTGCCGACA TAGCAGAATCGGCATCACTAGGCAACGTAGAGGTAGGAACGGCGCCTCCAGTTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACGATAAGAACTTCAATGGCG AAGAGGATTGGCATCTGGGACAGGGAGTGTCCATCGAATGGAGACAGAAAAGCTATAGCACACAGGTGGACCCTGA CCTCGCCGATCAGCCTAGCCTCATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTTATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCATATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTCGCACTCAGTCAACCCACAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTTCCACTG AGCAGGCAAGACGAAGACGCAAGCCAAGTACCATAGCAATTGGAGAACCATTGGCAATGAGTTTAACCTCCCCCTA TCGTCCCTAAGGAAATCGTCGCAAATTGCAATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGATGAAGAGAT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCAACTGATTCACCTCCACTATTTCGATTGCTTTGCCGATAGCGC AATCCATCCCATCGGCCAACACGGAATGGAGGATGAGGATAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG TGAAACACTGGCCCCTCACCGAAGAGAAAATCAAAGCCATTTGGCCTAGCAACAAGGGAAGGCCTGGCAATTTCCC GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAGCTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGATAGCCGACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATATCCCAGGTGAACACGCTAA CATTCCTCCCATTGTGGCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGAGTGAGGCTATTCACGGA CAGGTGAACTGTAGCCCTTCCGAGGGAACAAGACAGACTAGGAAGAACAGACGTAGAAGGTGGCGTGCGAGGCAAA GGCAAATCCACTCCATCTCCGAGAGGATTCTGGGACAGATGAGGGAACCCAGAGGCTCCGACATTGCCGGTACTAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAGCAATCCCCCTAGCATTCAACAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTAAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACCATACCCAAGGCTATTTCCCTGACTGGCAGAATTACACCCCGGACCCGGAGTCAGATACCC TAGCAGAGAAAGACAGAGACAGATTCATTCTATTAACGAATGGATTCTCAGCAACTGCCTCGGCAGATCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGTCAAGAATTGGATGACCGAGA CACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGAGAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCCATCTG TGAAATGCAATAACAAAAGGTTCAACGGAACTGGACCCAGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTATCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCGGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATCATTA GGACATACTGGGGCCTCCACACAGGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGGGTGCTCAAGACCGGCAAGTACTCTAGGAAGAGG GGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGCTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTGGGGGAATCTGCTCCAGTACTGGGGCCAGGAACTGAAAATCTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGAGCTGCCTGAGAAAGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACCCCGGAAGAGCCATTGAGGCTCAGCAACACATGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATTGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAAATCAACAGGATAGGAATGAGAAAGACCTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTCTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA AACAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCGTA GCTCCCTGAAAGGCCTCCAGAGAGGCACACTGAATGCCTGGGTGAAAGTGATTGAGGAAAAGGGATTCAGTCCCGA AGTGATTCCCATGTTTTCCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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### B2 fragment

qqatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGACACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCATCTTTAGGCCTGGCGGAGGCAATATGAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGAGCCTATCGTTGGCGCTGAGCCTCAGGATC CGCTGTCCTGTTTCTGGATGGCATTAACAAAGCTCAAGAGGAACATGAGAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCGGCC TGTCAAAACCATTATCGTCCACCTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCAAGTGTCCTCAGCGGC GGCAAGCTGGACGCCTGGGAAAAGATTAGGCTCAGGCCTGGCGGCAAGAAAAAGTATAGGCTCAAGGAGAAGGAG GCCTGGACGGACTGATTTACTCCCAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCTTGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGGGGGGGGGACAGCTCCTGTCCGGCATTGTGCAACAGCAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACAGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGTCGGGAGTGGAAGCCCTCAAAAGCCCCAAAAAAGATTAAG CCTCCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAAATGGAATAAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTGTCGATATCATTGCAACCGACATTCAGACTAAGGAACTGCAAAACCAAATCATAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAATCATTGACATTATC GCCAGCGATATCGTTCCCGTGGGCGATATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATTCACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGATGCCCGC CCTCTGTCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAGCAAAAAGGCTAGTGGAGTGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGACCAGGCTGAGCACCTGAAAAACCGCTGTGCAAATGGC CCCATTGCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAGGATTGGCCCTGAGAATC CCTATAACACCCGTCTTTGCCATTCAAGTGAGAGACCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTCGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAACCTGCCGACA TAGCAGAATCGGCATCACTAGGCAACGTAGGAGGTAGGAACGGCTCCTCCAGGTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACAATAAGACATTCAATGGCG AAAAGGATTGGCATCTGGGACAGGGAGTGTCCATCGAATGGAGAAAGGAAAAGCTATAGCACACAGGTGGACCCTGA CCTCGCCGATCAGCCTAGCCTCTATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTCATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCAAATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTTGCACTCAGCCAACCCCAAAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTACCACTG TCAGGTCTGCTTCCTGAAGAAGGGACTGGGGAATCAGGGATTACGGAAAGCAAATCGCTGGCGCTGACTGTGGCCC AGCAGGCAAGACGAAGACGCAAGCCAAGTACCATAGCAATTGGAGAACCATGGCCAGTGAGTTTAACCTCCCCCCTA TCGTCGCTAAGGAAATCGTCGCAAGTTGTGATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGCTGAAGAGCT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCATCTGATTCACCTCCACTATTTCGATTGCTTTTCCGATAGCGC AATCCATCCCATGGGCCTACACGGAATGGAGGATGAGGAAAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAACTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGAAAGCCAACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCAGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATGTCCCAGGTGAACACGCTAA CATTCCTCCCATTGTGCCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGGGTGAGGCTATGCACGGA CAGGTGGACTGTAGCCCTTCCGAGGGATCAAGACAGGCTAGGAAGAACAGACGTAGAAGGTGCCGTGAGAGGCCAAA GGCAAATCCGCGCCATCTCCGAGTGGATTCTGGGACAGATAAGGGAACCCAGAGGCTCCGACATTGCCGGTACCAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAACAATCCCCCTGGCATTAAGCAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACAATACCCAAGGCTTTTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAATCAGATACCC TAGCAGAGCAAGACAGACAGATTCATGCTATTAGCGAAAGGATTCTCAGCAACTTCCTCGGCAGACCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGACA CACTGCTCGTGCAAAACGCAAACCCTGACTGTGAGAAAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCGATCTG TGAAATGCAATAACAAAAAGTTCAACGGAACTGGACCCTGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTGTCTCCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGAGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCAGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCGTCATTA AGACATACTGGGGCCTCCACACAGGGGGTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGGAGTGCTCAAGACCGGCAAGTACTCCAGGATGAGG AGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGTTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTTGTGGAATCTGCTCCTGTACTGGGGCCTGGAACTGAAAAACTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGTGCTGCCTGAGAAAGAAGGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACGCCGGAAGAGCCATTGAGGCTCAGCAACACTTGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATCGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGCAAGAACTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGCCGTTTTTTTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA CAGAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCATA GCTCCCTGAGAGGCCTCCGGAGAGGCACACTGAATGCCTGGGTGAAAGTGGTTGAGGAAAAGGGATTCAATCCCGA AGTGATTCCCATGTTTACCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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### C1 fragment

ggatccaccATGCTCGAGAGCAACACCCCGCTAATAATGCCGATTGCGCGTGGCTGAAAGCCCAGGAAGAGGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCTTGGAGGGCTATCCTCAACATTCCCAGGAGGATTAGGCA AGGCTTTGAGAGAGCCCTCCTAGCCGCCGAATGGGACAGGGTTCACCCTGTGCACGCTGGCCCTGTCGCTCCCGGC CAAATGAGAGAGCCCAGAGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGAAGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CAAGGCCAATGGACCTACCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATTCCAGAATGAGAA GCGCTCACACAAACTGGATGACAGAAACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAGGGC TCTGGGAACCGGAGCCACACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATACGATGCTCAACATCGTCAGCGGACACCCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGAC CAAAAGGAAACCTGGGAGGCTTGGTGGACGGAATACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATA CCCTCCCTCGTGTTTCCCGATTGGCATAACTATACCCCTGGCCCTGGCATAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGAACCCATTGTCGGAGCCGAAACC TTTTACGTGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGGCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCGTCGAAGAGAAAGCCTTTAACGAAACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCGTACCGATCCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAAATCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCAAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGACGGCTCTGATTAAGCCTAAGAA **AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG** CCTAACAATAACACAAGGAAAGCCGCCGCTAGTGAAGTACGGAATAAGTCCAAACAGAAAACCCAGCAAGCTGCCG CCGATACAGGCGACTCCAGCCAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCAAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGAGTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCAATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAACCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCCTCACCTCCACAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGTTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACCCCTAAGTTTAAGTTCCCCATTCAGAAAGAGACATGGGAAGCCTGGTGGACGGAGTATTGGCAAGCCGCTGCTT ACAGACTGATCAGCTGTAACACAAGCGTTATCAAACAGGCTTGCCCTAAGATTACCTTTGACCCTATCCCTATCCA TTACTGTGCCCCTCCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGACTCCTGGACAGTGAATGACATTCAGAAATCAATTCTGAGAGCCCTCGGCCCAGGCGCTTCCCTGGAGG AAATGATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGATAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATGAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGTTTCTGGGACTCTGGGG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATATTATCTGTACCACAACCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTCAATGGCTGATTCTCGCTATCGTCGTGTGGACCAT TGTGTATATCGAATACAAGAAACTGCTCAGGCAAAGGAGAATCGATAGGCTCATCAAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACACCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA CCCATTTCCAAAGCTCCATGACCCAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTAGAGAGACCTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGAAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTATCCTCAAGA TTAAGCCTGTGGTCAGCACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCGATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACGCTGGCATCAAAGTGAAGCAACTG ATGTGAATGCTGCTCAAACCAGAGGCGATAACCCTACCGGTCCCGAAGAGTCCAAGAAGAGGTCGCGTCCAAGAC AGAGACAGACCCTTGTGACGCCCCCTAGCTCCAACTTTCTGGGAAGGTCTGCCGAACCCGTCCCCTCCAGCCC GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACTCACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGGGGGGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGTGAAGTGCAACTGGGAATCCCTCACCCTGCTGGACT GAAGAAAAAAGTCAGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAGACAGCTCTGCAAACTGCTCA GGGGTACAAAGGCTCTGACAGAGATTGTGACACTGACAGAGGAAGCCGAACTGCACATATGGAAGTTTGA CTCCCGCCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTTCTACAAAGACTGCGCTGCTGTCGAGCTC CTGGGACGCTCCAGCCTCAAGGGACTGCAAAGGGGATGGGAAGGCCTCAAGTATTTGTGGAACCTCCTGCAGTATT GGGGCTCTAGCCTGGGGCAACTGCAACCTGCTCTGAAAACCGGATCAGAGGAACTGAAGTCCCTGTATAACACAAT CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCAAACCCCTCGGCATTGCCCCT ACCAGAGCCAAAAGGAGAGTGGTCGAGAGAGAGAAAAGGCTCACCGAAATCGTCCCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAGGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGTCAACAATGCCAACATCATGATGCAGAGGGCAATTTCAAAGGGCCTAAAGAGAATCATCAAACAAGAGGAA GAGGAGGTCGGCTTCCCCGTCAGGCCCCAGGTCCCACTGAGACCTATGACCTACAAAGGAGCCGTCGATCTGTCCT TCTTCAGACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAAATACAAAATGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT CCGAGTCCGAGCTCGTGAATCAGATTATCGAAGAGCTCATCAAGAAGATTGCCGTCGCCGGATGGACAGAAT GGGCTGATGTGAAACAGCTCACCGCAGTCGTCCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACGCC CAAGTTCAGACTGCCTATCGCTGCCGCCAGCAACGAGAACATGGAGACCATGGCTGCTtgaagatctgaattc

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### C2 fragment

ggatccaccATGCTCGAGAGCAACACAGCCGCTAACAATACCGATTGCGTGTGGCTGAAAGCCCAGGAAGAGAGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCGGGAGGGCTATCCTCAACATTCCCACGAGGATTAGGCA AGGCCTTGAGAGAGCCCTCCTAGCCGCCGAATGGGATAGGATTCACCCTGTGCACGCTGGCCCTATCGCTCCCGGC CAAATGAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGATGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CGAAGACCAAAGCTCTCAGAGAGAGCCTTACAATGAGTGGACCCTGGAGGCTCCTGGAAGAGCTCAAGCACGAGGCT CAAGGCCAATGGACCTTCCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATGCCAGAATGAGAG GCGCTCACAAACTGGATGACAGATACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAAGGC TCTGGGACCCGGAGCCTCACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATATGATGCTCAACACCGTCGGGGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGGC CAAAGGGAAACCTGGGAGGCTTGGTGGATGGAATACTGGCAGGCTACCTGGATTCCTGAGGGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCAAAACTATACCCCTGGCCCTGGCACAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGACCCCATTGTCGGAGTCGAAACC TTTTACGCGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGCCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCATCGAAGAGAAAGGCTTTAGCGACACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCCTACCGATCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAACTCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCCAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGAAGGCTCTGATTACGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCGATACAGGCAGCTCCAGCAAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCGAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGAAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGATTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCGATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAGCCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCATCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGCTGTCCTCGGCTCCACCGTCATCTGGGGTAAA ACAGACTGATCAGCTGTAACACAAGCGTTATCACACAGGCTTGCCCTAAGATTAGCTTTGAGCCTATCCCTATCCA TTACTGTGCCCCTCGTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGAGTCCTGGACAGTGAATGACATTCAGAAAACAATTCTGAAAGCCCTCGGCCCAGGCGCTACCCTGGAGG AAAATATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGAAAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATCAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGCTTCTGGGAATCTGGAG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATCTTATCTGTACCACAGCCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTGAATGGCTGATTATCGCTATCGTCGTGGGACCAT TGTGTTTATCGAATACAAGAAACTGCTCAGGCAAAGGAAAATCGATAGGCTCATCGAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA GCCATTTTCCAAAGCTCCATGACCAAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTGGAGAGACTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTCTCCTCAAGA TTAAGCCTGTGGTCAGCACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCAATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACCCTGGCATCAAAGTGAGGCAACTG AGAGACAGACCCTTTTGACGCCGCCCCTAGCTCCACCTTTCTGGGAAGGTCTGTCGAACCCGTCCCCCTCCAGCTC  ${\tt CCCCTCTGGAAAGGCTCCACCTCGACTGTAGCGAAGACAGTGACGAACTGGATAAGTGGGCCTCCCTGTGGAACT}$ GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACCAACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGAGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGGGAAGCGCAACTGGGAATCCCTCACCATGCTGGACT GAAAAAGAAAAAGTCCGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAAACAGCTCTGCAAACTGCTCA GGGGTGCAAAGGCTCTGATAGACATTGTGCCACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCACCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTACTACAAAGACTGCGCTGCTGTCGAGCTC  $\tt CTGGGACGCTCCAGGCACTGCGAAGGGGATGGGAAGCCCTCAAGTATTTGTGGAACCTCCTGCAGTATT$ GGGGCTCTAGCCTGGAGCAACTGCAATCTGCTCTGAAAACCGGATCAGAGGAACTGAGGTCCCTGTTTAACACAGT CGCTACCCTCTGGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCGAACCCCTCGGCATTGCCCCT ACCAAAGCCAAAAGGAGAGTGGTCCAGAGAGAGAGAAAAGGCTCACCGATATCGTCACCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAAGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGCCAACAATGCCAACATGATGCAGAGAGGGCAATTTCAGAGGCCCAAAGAGAATCATCAAACAAGAGGAA GAGGGGGTCGGCTTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGCAGCCATCGATCTGTCCT TCTTCAAACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGATCTGGTGGCAAAAAGAAATACAAACTGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT GGGCTGATGTGAAACAGCTCACCGAAGTCGTTCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACACC CAAGTTCAGACAGCCTATCGCTGCCGCCAGCAACGAGAACATGGACGCCATGGCTGCTtqaaqatctgaattc

### INTERNATIONAL SEARCH REPORT

International application No.

### PCT/AU01/00622 CLASSIFICATION OF SUBJECT MATTER Int. Cl. 7: C07K 19/00; C12Q 1/68; C07K 2/00, 14/005, 14/15, 14/20, 14/435; C12N 15/09 According to International Patent Classification (IPC) or to both national classification and IPC FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) SEE ELECTRONIC DATABASES BELOW Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SEE ELECTORNIC DATABASES BELOW Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CA WPIDS MEDLINE: Combinatorial protein/peptide/polypeptide; gene/DNA shuffling; domain swapping; vaccine; synthetic protein/peptide polypeptide DOCUMENTS CONSIDERED TO BE RELEVANT C. Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category\* WO 00/18906 A. MAXYGEN INC. 6/4/00 All X All WO 99/41402 A. MAXYGEN INC. 19/8/99 X All WO 99/41369 A. MAXYGEN INC. 19/8/99 X WO 99/41368 A. MAXYGEN INC. 19/8/99 All X All Ryu DDY and Nam D-H. Recent progress in biotechnological engineering. X Biotechnol Prog. Jan-Feb 2000. 16: 2-16. All X Punnonen J. Molecular breeding of allergy vaccines and antiallergic cytokines. Int Arch Allergy Immunol. March 2000. 121: 173-182 See patent family annex Further documents are listed in the continuation of Box C |X| later document published after the international filing date or priority date and not in conflict with the application but cited to "A" understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot "E" be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such "O" combination being obvious to a person skilled in the art document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search Authorized officer Name and mailing address of the ISA/AU **AUSTRALIAN PATENT OFFICE** PO BOX 200, WODEN ACT 2606, AUSTRALIA Gillian Allen E-mail address: pct@ipaustralia.gov.au Telephone No: (02) 6283 2266 Facsimile No. (02) 6285 3929

### INTERNATIONAL SEARCH REPORT

International application No.

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# INTERNATIONAL SEARCH REPORT Information on patent family members

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This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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	EP 1054973		
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			EP 1056842

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